A Dissertation on

"COMPARISION OF CARCINOMA BREAST IN PRE-MENOPAUSAL AND POST-MENOPAUSAL WOMEN"

BY

DR. M. SURESH

DISSERTATION SUBMITTED FOR THE DEGREE OF

MASTER OF SURGERY

BRANCH-1 (GENERAL SURGERY) AT

MADRAS MEDICAL COLLEGE, CHENNAI

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY

GUINDY,

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CERTIFICATE

This is to certify that, the dissertation entitled "**COMPARISION OF CARCINOMA BREAST IN PRE-MENOPAUSAL AND POST-MENOPAUSAL WOMEN"** is the bonafide work done by **Dr.M.SURESH,** during his M.S., General Surgery course 2010-2013, done under my supervision and is submitted in partial fulfilment of the requirement for the M.S.,(BRANCH 1)- General Surgery of The Tamilnadu Dr.M.G.R.Medical University, April 2013 examination.

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DECLARATION

I **Dr.M.SURESH,** certainly declare that this dissertation titled **"COMPARISION OF CARCINOMA BREAST IN PRE-MENOPAUSAL AND POST-MENOPAUSAL WOMEN"** represents a genuine work of mine. The contributions of any supervisors to the research are consistent with normal supervisory practice, and are acknowledged. I also affirm that this bonafide work or part of this work was not submitted by me or any others for any award, degree or diploma to any other university board, either in India or abroad. This is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the rules and regulations for the award of Master of Surgery degree Branch 1 (General Surgery).

Dr.M.SURESH

Date :

Place :

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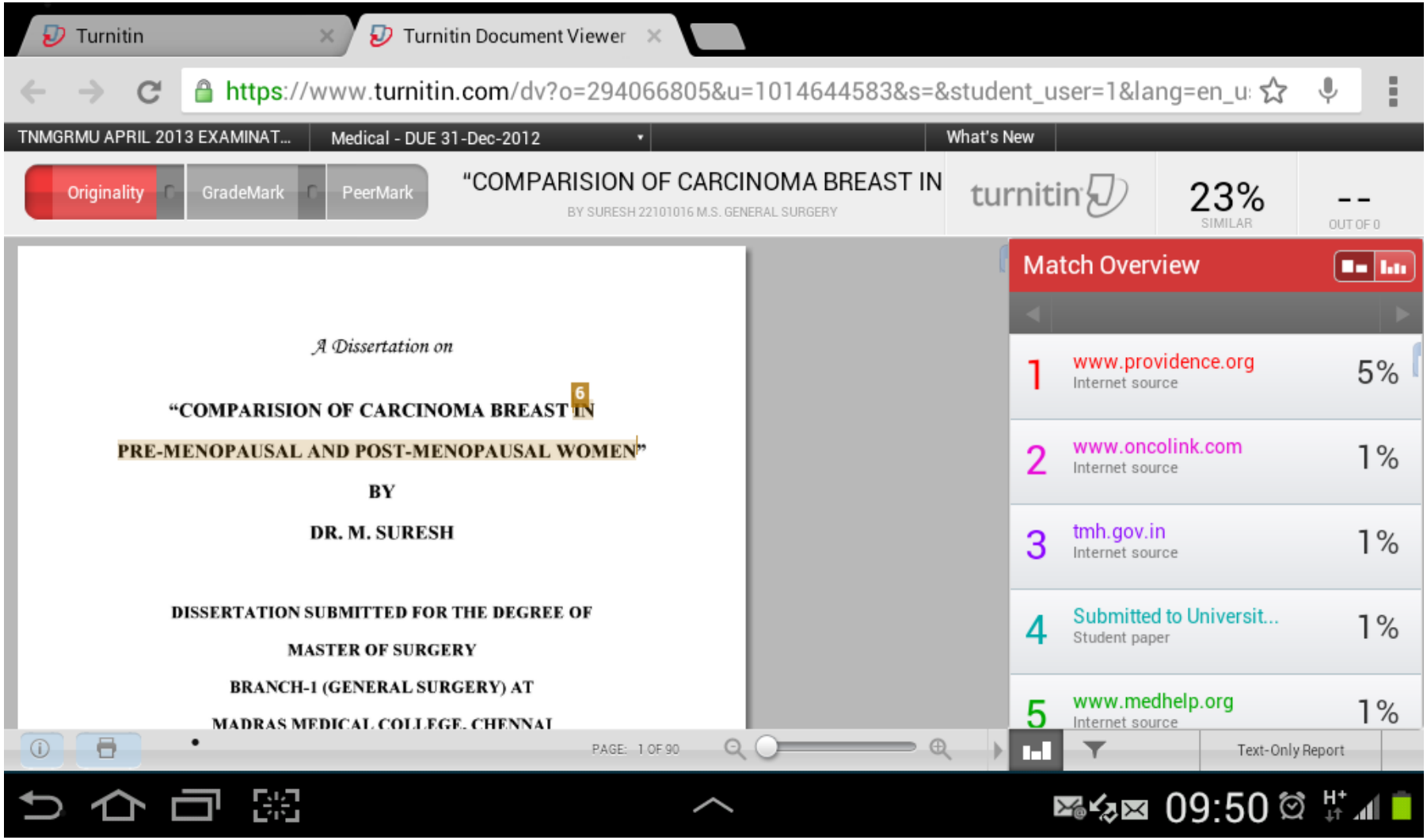
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CONTENTS

INTRODUCTION

Breast cancer is the most common of all cancers and is the leading cause of cancer deaths in women worldwide, accounting for >1.6% of deaths and case fatality rates are highest in low-resource countries. A recent study of breast cancer risk in India revealed that 1 in 28 women develop breast cancer during her lifetime. This is higher in urban areas being 1 in 22 in a lifetime compared to rural areas where this risk is relatively much lower being 1 in 60 women developing breast cancer in their lifetime. In India the average age of the high risk group is 43-46 years unlike in the west where women aged 53-57 years are more prone to breast cancer.

The overall incidence of breast cancer has been rising because of increases in the average life span, lifestyle changes that increase risk for breast cancer, and improved survival from other diseases. Despite an increasing incidence, mortality from breast cancer has continued to fall, thought to be the result of both earlier detection via mammographic screening and improvements in therapy. Current treatment of breast cancer is guided by recent insights into breast cancer biology, an increasing ability to define disease biology and status in individual patients, and the availability of improved treatments.

This is a prospective study conducted at RGGGH. All patients suspected to have breast cancer undergo detailed clinical examination. Routine investigations, FNAC/core-cut biopsy, Mammogram, USG abdomen, bone scan are taken to aid in the diagnosis. Staging of the malignancy in done according to the AJCC Classification. Tumors were subjected to Histopathological examination after surgery and ER and PR status checked**.**

AIMS AND OBJECTIVES

COMPARISION OF CARCINOMA BREAST IN PRE-MENOPAUSAL AND POST-MENOPAUSAL WOMEN

1. To compare the clinical stage at presentation.
2. To compare Body Mass Index [BMI].
3. To compare the incidence of various pathological types of carcinoma breast.
4. To compare ER and PR status.
5. To compare associated proliferative breast diseases.
6. To compare incidence of mammographic abnormalities in contralateral breast.

REVIEW OF LITERATURE

BRIEF SURGICAL HISTORY OF BREAST :

- In 1600 B.C. Ebers Papyrus (Egypt) suggested Heat cauterization and Excision of Breast tumors by knife.

- In 525 B.C. Democedes successfully treated a woman with Breast tumor.

- In 460 - 377 B.C. Hippocrates made detailed references to Breast cancer and its effects.

- In 130 – 200 A.D. Galen claimed an excess of black bile (melancholia) caused cancer. Treatment centered on nutrition and purgation. Surgical excision was only recommended if tumor was removable.

- In 1514-1564 Andreas Vesalius did wide excision and used ligatures for hemostasis.

- In 1510-1590 Pare recognized relationship between breast cancer and axillary node involvement.

- In 1786 Cruikshank described lymphatic drainage of Breast.

- In 1845 Astley Cooper identified Suspensary ligaments of Breast which were named after him.

- In 1867 Moore argued that local recurrence after Breast amputation was due to disseminated fragments not removed at the time of surgery. He suggested removal of Breast along with surrounding tissue.

- In 1870 Lister described antiseptic principles, supported and refined Moore's technique of axillary exposure and divided pectoral muscles.

- In 1875 Volkmann proposed wide excision of Breast, skin and pectoral fascia. In advanced cases he removed pectoralis major muscle and sometimes pectoralis minor muscle.

- In 1878 Billroth did Lumpectomy for early Breast cancer.

- In 1882-1907 Halsted described Radical mastectomy. He did axillary clearance in all cases and also removed pectoralis major in most of them giving wide margin of clearance.

- In 1885 Sappey noted the presence of subareolar plexus into which parenchymal lymphatics drained, claiming that most of drainage was to axilla.

- In 1891 Welch used frozen sections in diagnosis of breast cancer.

- In 1895 Czerny replaced surgically removed breast with large lipoma (breast reconstruction).

- In 1896 Tansini performed immediate breast reconstruction using latissimus dorsi musculocutaneous flap after radical mastectomy.

- In 1897 Gocht irradiated a case of inoperable breast cancer (Roentgen's x-rays were discovered in 1895).

- In 1899 Rotter noted metastases while tracing lymphatics from breast to inter-pectoral nodes.

- In 1918 Stibbe published detailed study on internal mammary lymphatics.

- In 1927 W.S. Handley suggested standard radical mastectomy be extended to include internal mammary lymphatics. Also implanted radium tubes parasternally as prophylaxis.

- In 1938, Gershon-cohen recommended screening for breast cancer.
- In 1943, Patey and Dyson developed modified radical mastectomy. Advocated wide skin excision and axilla clearing while sparing pectoralis major muscle.
- In 1948 McWhirter promoted combination of simple mastectomy and high voltage x-ray therapy.
- In 1960, Egan described modern mammography.
- In 1963, Gros proposed "senology" as special discipline for study of breasts.
- In 1963 Dodd et al. did First needle-localization procedure. Published in 1965.
- In 1964, Witten stated that 80-90% of breast cancer determined by surgical biopsy can also be discovered from mammography.
- In 1965, Auchincloss and Madden described radical mastectomy preserving both pectoralis major muscles.

- In 1971, Fischer and NSABP members initiated protocol B-04 comparing radical mastectomy plus radiotherapy and total mastectomy alone.

- In 1976, NSABP protocol B-06 was started. It compared total mastectomy, lumpectomy plus irradiation and lumpectomy alone.

- In 1977, Dreaver pioneered breast reconstruction with myocutaneous flaps. Published in major journals in 1981, 1986.

- In 1978, Bostwick described and popularised use of latissimus dorsi myocutaneous flap.

- In 1981, Turner and Maddox reported on the Manchester and University of Alabama trials of radical versus modified radical mastectomy, finding no difference in survival.

- In 1992-1994 Krag and Guiliano published development of sentinel lymph node mapping for carcinoma Breast.

- In 1995, genetic mutations causing breast carcinoma were identified, named as BRCA-1 and BRCA-2 by researchers.

- In 1997, March et al. Joint Task Force conducted National surveys of breast core biopsy use.

- In 2007, Bevacizumab, monoclonal antibody directed against VEGF was introduced as adjuvant treatment for carcinoma breast.

EPIDEMIOLOGY OF BREAST CANCER :

- Breast cancer is the most common neoplasm in women, accounting for 26% of cancers diagnosed annually.

- It is overall the second leading cause of deaths due to cancer following lung cancer, and in women >65 years it is the leading cause of death.

- The incidence of breast cancer is highest among women of higher socio economic background.

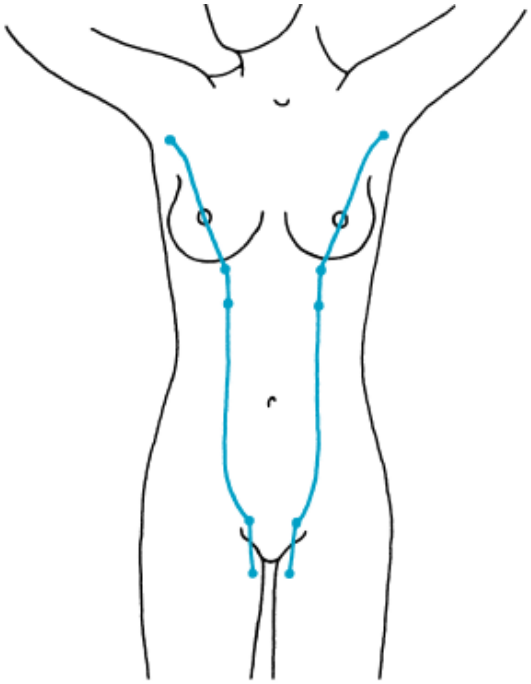
- Over the last 10 years mortality due to breast cancer has been steadily decreasing most likely due to early detection and improved efficacy of adjuvant therapies.

- The lifetime risk of an Indian woman developing breast cancer is 1 in 28. It is higher in urban women as compared to rural women.

- The incidence of breast cancer in Indian population as per 2006 is 20.01 per 1,00,000 population and mortality is 4.32 per 1,00,000 population.

EMBRYOLOGY :

LINE OF SCHULTZ



- The breast is a group of large glands derived from the epidermis.

- During the second month of gestation, two bands of slightly thickened ectoderm appear on the ventral body wall extending from above the axilla to below the groin.

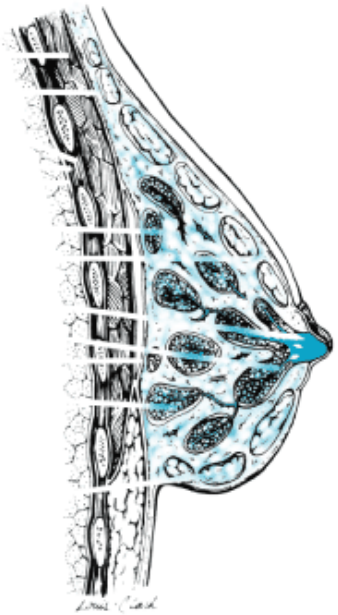
- In humans, only the pectoral portion of these bands will persist and ultimately develop into adult mammary glands.

- The glandular portion of the breast develops from the ectoderm. It arises from the local thickening of the epidermis. From this

thickening, 16 to 24 buds of ectodermal cells grow into the underlying mesoderm (dermis) during the twelfth week. These buds, at first solid, will become canalized near term to form the lactiferous ducts

- The connective-tissue stroma of the breast forms from the mesoderm, which will form the dermis of the skin and the superficial fascia (tela subcutanea) as well. Fibers forming the suspensory ligaments (of Cooper) will develop from both layers. This development, as well as the appearance of fat in the superficial fascia, does not occur until puberty in the female

ANATOMY OF BREAST:



- The breast lies in the subcutaneous plane over the pectoral region, base extending from midline to anterior or midaxillary line and 2nd to 6th ribs, nipple approximately situated at the level of 4th intercostal space.

- It overlies the pectoralis major, serratus anterior and to some extent the rectus sheath and external oblique muscle

- The breast is separated from the underlying muscles by a condensation of superficial fascia, called pectoral fascia.

- A small extension into the upper quadrant reaching the medial wall of axilla is known as the Axillary tail of Spence, which is often poorly connected with the ductal system.

- Its clinical significance lies in that the swellings arising from this tail, may be readily mistaken for lymph nodes.

- The axillary tail of Spence enters the axilla through an opening in the pectoral fascia known as the foramen of Langer, at the level of the 3rd intercostal space.

- About 20 lactiferous ducts converge radially to open on the nipple, a cylindrical projection on the summit of the breast.

- The nipple is surrounded by circular pigmented skin called as the Areola.

- Sebaceous glands under the areola form small elevations, known as Montgomery's tubercles.

- Fibrous septa running between the skin and pectoral fascia called as the Suspensory ligaments of Cooper, through the mammary tissue help to maintain their shape in young breasts and their atropy in elderly account for the sagging of their breasts.

- These septa also explain skin tethering in early malignancy and orange peel appearance in diseases that produce cutaneous lymphedema.

ANATOMY OF AXILLA :

- It is a pyramidal space wedged between the upper arm and the side of the chest and ceases to exist when the arm is hyperabducted.

- It is limited by anterior and posterior folds, communicating above with the supra clavicular fossa, through the apex which transmits the neurovascular and lymphatic structures.

- The anterior wall is formed by pectoralis major, minor, subclavius and clavipectoral fascia.

- The posterior wall extends lower and is formed by subscapularis, teres major and latissimus dorsi.

- The lateral wall is the narrowest, since the anterior and posterior walls converge to the lips of the bicipital groove, this is formed by the upper humerus, coraco-brachialis, biceps muscles and the axillary neurovascular structures.

- Medially it is bounded by the upper five ribs, the intercostals and upper digitations of serratus anterior muscle.

- The floor is formed by the axillary fascia, bridging from fascia over the serratus anterior to the deep fascia of the arm.

- The action of pectolralis major is adduction and internal rotation of the shoulder, the former is employed to put the muscle into contraction, to detect fixity of a breast mass.

NORMAL DEVELOPMANT AND PHYSIOLOGY :

- The breast development begins between the ages of 9 and 12. The events are initiated by low amplitude pulses of pituitary gonadotropins, which raise serum oestradiol concentration.

- In breast this hormone dependent maturation entiles increased deposition of fat, the formation of new ducts by branching and elongation and the appearance of lobular units.

- This process is controlled by pituitary hormones, progesterone, oestrogen, adrenal hormones and effects of thyoid hormones and insulin.

- The mature post pubertal breast contains stroma, lobular units, lactiferous ducts and fat. During phases of menstrual cycle or in response to exogenous hormones, the breast stoma and epithelium of lobules undergo cyclic stimulation. The main process is not hyperplasia but alteration of morphology and hypertrophy, In late luteal phase there is fluid accumulation and intralobular oedema which are reasons for breast engorgement and pain

- Although minor changes occur during each menstrual cycle, pregnancy and lactation bring about the ultimate development of

the breasts. Progesterone, prolactin, and placental lactogen are key hormones in stimulating the formation of secretory alveoli which develop at the ends of the branched ducts. As development continues, the cells of the secretory alveoli acquire increased organelles related to protein synthesis and secretion.

- During lactation, prolactin from the anterior pituitary gland causes mammary glands to secrete milk proteins and lipids. Milk ejection occurs in response to the neural impulses elicited by sucking activity at the breast. This stimulus causes release of oxytocin by the paraventricular nuclei of the hypothalamus via the posterior pituitary gland. These neural impulses also inhibit the release of luteinizing hormone.

- When nursing ceases, prolactin secretion is reduced. Nonejected milk in the alveoli effects the cessation of milk production. The alveoli regress, and the duct system regresses to the nonpregnant state.

BLOOD SUPPLY :

- The lateral thoracic artery from the 2nd part of axillary artery

- The perforating cutaneous branches of internal mammary artery to the 2nd, 3rd, and 4th intercostal spaces.

- The lateral branches of the 2nd, 3rd and 4th intercostal arteries.

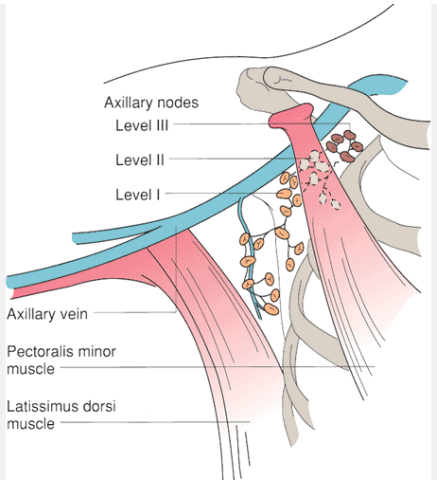
- Pectoral branches of acromio-thoracic artery.

VENOUS DRAINAGE :

- The superficial veins from the breast characterised by their proximity to the skin drain to the axillary, internal mammary and intercostal vessels.

- Through posterior intercostal veins, venous drainage communicates with the paravertebral venous plexus. So secondaries in vertebrae are common in carcinoma of the breast.

LYMPHATIC DRAINAGE :



- **Level 1 –** Lymph nodes lateral to pectoralis minor muscle.
- **Level 2 –** Lymph nodes deep to pectoralis minor muscle.
- **Level 3 –** Lymph nodes medial to pectoralis minor muscle.
- Lymphatic drainage of breast is of great clinical significance, outer quadrants predominantly draining into axillary and inner quadrants into internal mammary group of nodes on the same side.
- However when these channels are blocked, alternate drainage pathway may take place, into supraclavicular nodes, opposite breast and axilla, peritoneal cavity and liver via rectus sheath and falciform ligament.
- The lymphatics of nipple and areola drains into subareolar plexus of Sappey, before they reach the regional nodes.

The Axillary lymph nodes numbering around 50 are grouped as follows

Anterior or Pectoral group,

- Located under the anterior axillary fold

Posterior or Subscapular Group,

- Located in the posteromedial wall of axilla, in relation to the posterior fold

Lateral group,

- Along the axillary vessels

Apical group,

- Which form the junction between the axillary and supraclavicular chains,

Deltopectoral group,

- Located above / medial to the pectoralis minor, in relation to the clavipectoral fascia.

Interpectoral group,

- Located between pectoralis minor and major muscles

ANOMALIES OF BREAST :

One or both breasts may be hypoplastic due to under development of the lactiferous apparatus or grossly hypertrophied and pendulous (gigantomastia).

Amastia – absence of breast, may be seen in Turner syndrome and congenital adrenal hyperplasia or tumors. Absence of a breast, sterno-costal head of pectoralis major muscle, syndactylism and nephropathy is known as Poland syndrome.

Athelia – absence of nipple.

Polymastia or polythelia – supernumerary breasts or nipples might develop along the milk line, most often in the inframammary regions, due to incomplete involution of the mammary ridge (milk line)

ABERRATIONS OF NORMAL DEVELOPMENT AND INVOLUTION (ANDI) :

It occurs due to a disturbance in the cyclical hyperplasia or involution changes that occur in the breast, often bilateral.

It is seen in the 3rd and 4th decades of life and is common in spinster, nullipara and those who have not breast fed their children.

The pre-menstrual accentuation of subjective or objective features favour a hormonal hypothesis, supported by the relief of symptoms by cyclical hormonal treatment, however their precise role is ill understood.

Its pathogenesis is not clear and wide range of processes occur such as fibrosis, adenosis, epitheliosis, cystic changes and inflammation, in varying proportions and combinations.

The process starts with periductal fibrosis, probably secondary to oestrogen stimulation, which causes irritation of the cells lining the ducts and increased epithelial proliferation (epitheliosis)

Progressive epithelial clumping gives a gland like appearance (adenosis) and obstruction to the ductal drainage causes the cystic changes

The pre-malignant potential of fibroadenosis is debatable and the higher incidence of malignancy seen in this disease may be related to continued oestrogen influence, which is a common denominator to both the conditions.

EARLY REPRODUCTIVE YEARS (AGE 15–25)

NORMAL

* Lobular development
* Stromal development
* Nipple eversion

DISORDER

* Fibroadenoma
* Adolescent hypertrophy
* Nipple inversion

DISEASE

* Giant fibroadenoma
* Gigantomastia
* Subareolar abscess

LATER REPRODUCTIVE YEARS (AGE 25–40)

NORMAL

* Cyclical changes of menstruation
* Nodularity
* Epithelial hyperplasia of pregnancy

DISORDER

* Cyclical mastalgia
* Bloody nipple discharge

DISEASE

* Incapacitating mastalgia

INVOLUTION (AGE 35-55)

NORMAL

* Involution of lobules
* Involution of ducts
* Epithelial turnover

DISORDER

* Duct ectasia
* Nipple retraction
* Epithelial hyperplasia

DISEASE

* Periductal mastitis
* Epithelial hyperplasia with atypia

RELATIVE RISK FOR THE DEVELOPMENT OF BREAST CANCER IN ANDI

Non proliferative : No Increased Risk

* Microcysts / macrocysts
* Ectasia of ducts
* Simple fibroadenoma
* Mastitis
* Fibrosis
* Apocrine metaplasia or squamous metaplasia
* Mild hyperplasia

PROLIFERATIVE : RR 1.5 TO 2.0

* Complex fibroadenoma
* Papilloma
* Sclerosing adenosis
* Hyperplasia; moderate or severe

PROLIFERATIVE WITH ATYPIA: RR 4.5 TO 5.0

* Atypical ductal hyperplasia
* Atypical lobular hyperplasia

RISK FACTORS FOR DEVELOPMENT OF BREAST CANCER:

RELATIVE RISK < 2

* Early menarche
* Late menopause
* Nulliparity
* Estrogen plus progesterone
* Hormone replacement therapy
* Alcohol use
* Post-menopausal obesity

RELATIVE RISK 2 TO 4

* One first degree relative with breast cancer
* CHEK 2 mutation
* Age > 35 years at first child birth
* Proliferative breast disease
* Mammographic breast density

RELATIVE RISK >4

* Mutation - BRCA-1 or BRCA-2
* LCIS
* Atypical hyperplasia
* Radiation exposure before 40

PATHLOGY OF BREAST CANCER :

Invasive breast cancers constitute a heterogeneous group of lesions that differ with regard to their clinical presentation, radiographic characteristics, pathologic features, and biologic behavior. This classification scheme is based on the growth pattern and cytologic features of the invasive tumor cells

CLASSIFICATION OF BREAST CARCINOMAS :

NON-INVASIVE EPITHELIAL CARCINOMAS :

Lobular carcinoma in situ

Ductal carcinoma in situ, or intraductal carcinoma (papillary, cribriform, solid and comedo types)

INVASIVE EPITHELIAL CARCINOMAS :

DUCTAL

Invasive, NOS (Not Otherwise Specified)

Invasive with predominant intraductal component

Intraductal (in situ)

Comedo

Inflammatory

Medullary with lymphocytic infiltrate

Mucinous (colloid)

Papillary

Scirrhous

Tubular

Other

LOBULAR

In situ

Invasive with predominant in situ component

Invasive

NIPPLE

Paget's disease, NOS

Paget's disease with intraductal carcinoma

Paget's disease with invasive ductal carcinoma

OTHER

Undifferentiated carcinoma

The following are tumor subtypes that occur in the breast, but are not considered to be typical breast cancers:

Cystosarcoma phyllodes

Angiosarcoma

Primary lymphoma

DUCTAL CARCINOMA IN SITU :

Broder’s definition of DCIS still holds good, as the transformation of epithelial cells of any duct in the body into malignant cells, which however remain in the same normal anatomic position without having breached the basement membrane.

In the pre mammography era, DCIS was rarely diagnosed clinically. It presented as discharge from the nipple or in later stages as the Paget’s disease of the nipple, with a palpable mass.

But with the advent of mammography, there has been a big surge in the detection of DCIS, it is however not logical to adopt the same course of treatment to symptomatic and asymptomatic (mammographically detected) DCIS.

The commonest mammographic findings are calcifications (which originate from intraductal debris), necrotic tumor cells in the ductal epithelium and other tumor cell secretions. 10% may present as soft tissue abnormalies as in invasive carcinomas.

The degree of cellular atypia and the presence of necrosis are the main features that delineate the grades of malignancy.

For example a high grade lesion like comedo DCIS displays both atypia and necrosis. It is the necrotic debris within the ductal lumen that gives the appearance of comedone (black head).

The low and intermediate grades of DCIS such as the cribriform, micropapillary, papillary and circinate patterns, are associated with atypical cytology without necrosis.

Multiple areas of rounded spaces within a stratified ductal epithelium characterise the cribriform pattern, giving the appearance of a sieve.

In papillary type the duct is filled with complex papillary folds. This has to be distinguished from a benign papilloma.

The treatment of DCIS is controversial.

LOBULAR CARCINOMA IN SITU :

This has no characteristic clinical feature and is sometimes found incidentally in mastectomy specimens.

Its main properties are its high bilaterality (40%) and multicentricity (70%) and high risk (10 times greater than controls) of the subsequent development of invasive carcinoma in one or both breasts.

The duration required for the development of invasive carcinoma from LCIS may be greater than 10 years, but these lesions require close monitoring by half yearly clinical examination and annual mammography.

The advent of mammography has made the surveillance of these patients more comfortable and reassuring, but it is important that they are enlisted for a lifetime screening program, because with the passage of time the anxiety becomes less, but unfortunately the risks become more.

INVASIVE CARCINOMA :

When stromal invasion is detectable, the tumors come under this category.

By far the commonest variety is the invasive ductal carcinoma of non specific type referred to as the NOS (Not Otherwise Specified).

This forms >80% of all carcinomas of breast in which no specific pattern is detectable.

All the special subtypes form the remaining such as tubular, mucinous, medullary and invasive lobular which tend to be better differentiated and have better prognosis than the NOS.

This implies that most ductal carcinomas are undifferentiated and cannot be easily classified morphologically.

The tumor cells may be in groups, cords or glands. The amount of stroma ranges from none to abundant and its appearance from cellular to densely fibrous.

In some of the cases of abundant stroma, it may be difficult to identify the tumor (earlier called as the atropic scirrhous type)

The Bloom and Richardson grading to determine the degree of aggressiveness of tumor is based on

* The tendency of cells to form tubules

* The pleomorphism of the nucleoli

* Frequency of hyper chromatic nuclei

Other histologic types of invasive carcinoma,

Tubular carcinoma representing about 3-5 % of the invasive carcinoma shows the tumor cells differentiated into tubular pattern. In its pure form it rarely metastasises. No further therapy is required if these tumors are excised with a 2 cm of normal tissue in all the dimensions.

Cribriform carcinoma is another tumor which behaves biologically similar to tubular carcinoma.

Mucinous colloid carcinoma, in which pools of extracellular mucin are found in with an embedded aggregate of tumor cells. This comprises 2-4% of invasive carcinoma, usually presents in older women and carries an excellent prognosis.

Medullary carcinoma has solid sheets of large cells, associated with lymphocytic reaction.

Lobular carcinoma tends to be multifocal and also bilateral.

Inflammatory carcinoma has previously been ascribed to tumours occurring in pregnancy and during lactation (mastitis carcinomatosis), although it is now apparent that it occurs in all age groups. This type of breast cancer has previously been diagnosed on the pathological observation of tumour emboli in dermal lymphatics, although it is now defined by its clinical appearance with more than 50 per cent of the breast being red and warm in association with a brief history. This condition is associated with a poor prognosis, whether or not the dermal lymphatics contain tumour. Some studies have indicated an improved survival, however, if dermal lymphatics contain tumour (‘pathologically defined inflammatory breast cancer') but the clinical picture is absent.

Paget’s disease of the nipple, this type of breast carcinoma presents as a chronic eczema like lesion of the nipple / areola with nipple discharge. Upto 50% of patients have a palpable breast lump. It is seen in association with non invasive ductal carcinoma, which in due course turns invasive and may be limited to the ducts just beneath the nipple or sometimes beyond. Microscopically it is characterised by the presence of

large, ovoid cells with abundant clear pale staining cytoplasm in the Malpighian layer of epidermis. If eczema is not responding to conventional therapy within few weeks, skin biopsy must be done, as the prognosis is excellent, if treated before the mass is clinically felt, by wide local excision or mastectomy. With palpable mass it is treated as per the guidelines for other malignancies of breast.

CUTANEOUS MANIFESTATIONS OF CARCINOMA BREAST :

Peau d' orange

Due to obstruction in the dermal lymphatics, openings of sebaceous glands and hair follicles get buried in the oedema giving rise to the orange peel appearance.

Dimpling of skin

Due to infiltration of ligament of cooper

Retraction of nipple-

Due to infiltration of lactiferous duct

Ulceration and discharge from nipple or areola

Skin ulceration and fungation

Cancer en cuirasse

Skin over the chest wall and breast is studded with cancer nodule appearing like an armour coat.

Tethering to skin

SPREAD INTO DEEPER PLANE :

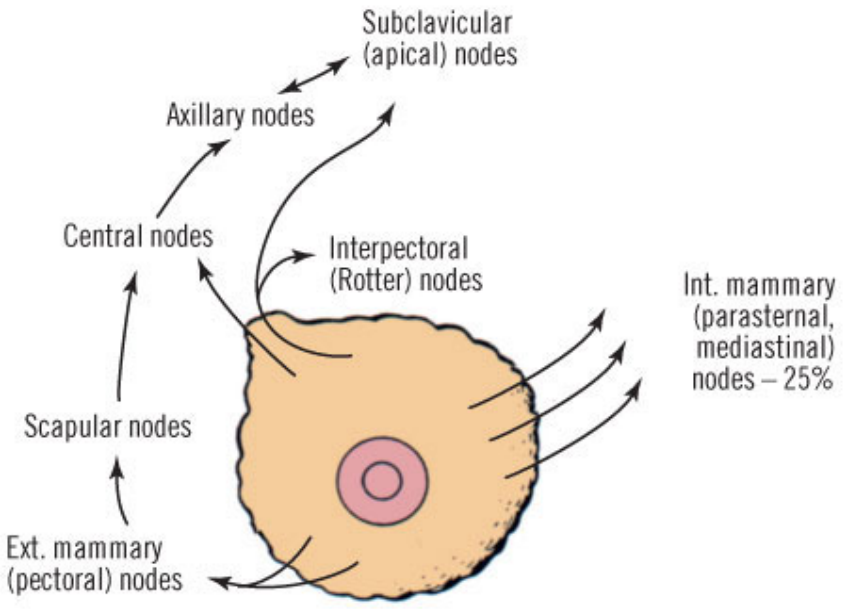
Into pectoralis major muscle is confirmed by observing the restricted mobility of the swelling while contracting the muscle.

Into latissimus dorsi muscle is confirmed by extending the shoulder against resistance.

Into serratus anterior muscle is confirmed by pushing the wall with hands without flexing the elbow.

Into the chest wall is confirmed that the breast will not fall forward while leaning forward and raising the arm above the shoulder, breast will not move upwards as it is fixed to the chest wall.

LYMPHATIC SPREAD :



Occurs through

* Subareolar sappey's lymphatic plexus
* Cutaneous lymphatics
* Intramammary lymphatics

Lymphatic spread almost always first occurs to the axillary lymph nodes.

From the axillary lymph nodes spread occurs to the supraclavicular lymph nodes by lymphatic embolization.

Through the dermal lymphatics it may spread to the contralateral breast or axilla.

* Spread restricted to level 1 nodes carries a better prognosis

* Spread to level 2 has poor prognosis.

* Spread to level 3 has the worst prognosis

Spread may occur to the internal mammary lymph nodes of the same side and then to the mediastinal lymph nodes.

Contralateral internal mammary nodes may also get involved by retrograde spread.

Fixed enlarged axillary nodes may cause lymphedema due to lymphatic block, venous thrombosis and venous oedema due to venous block and severe excruciating pain along the distribution of the median and ulnar nerves with often significant sensory and motor deficits due to tumor infiltration of the cords of brachial plexus.

HEMATOGENOUS SPREAD :

Bone

Commonest (70%), lumbar vertebrae, femur, ends of long bones, thoracic vertebrae, ribs, skull in order. They are osteolytic lesions often with pathological fractures. Present with painful, tender, hard, non-mobile swelling with disability. Spine secondaries can cause paraplegia.

Liver

Either through blood occasionally through trans coelomic spread.

Lung

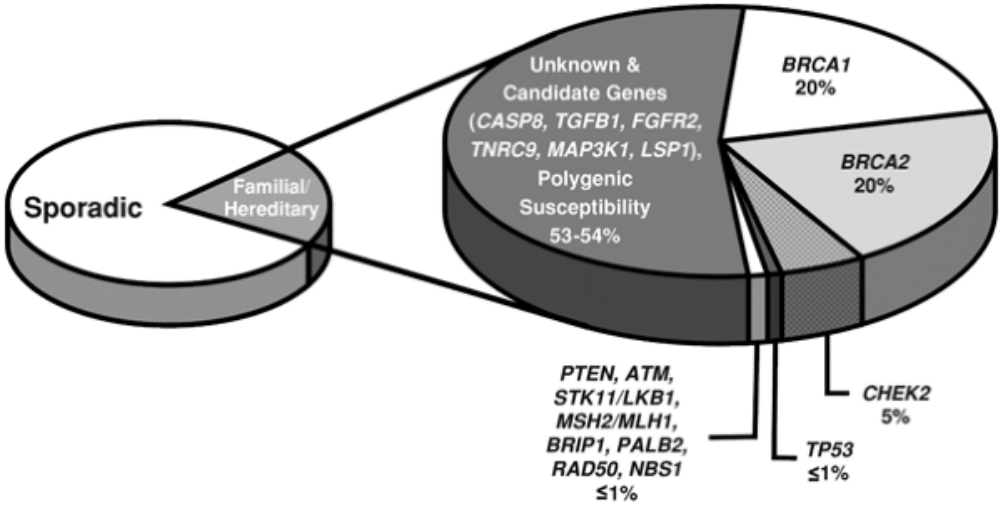
Causes malignant pleural effusion and cannon ball secondaries.

Brain

Causes increased intracranial pressure, coning.

Adrenals and ovaries.

GENETICS OF CARCINOMA BREAST :



About 5% of breast cancers are genetic, mutation of an autosomal dominant gene seems to account for the development of cancer.

The BRCA-1 found in the long arm of chromosome -17 is implicated in some breast cancers and has been recently cloned.

Some mutations in this gene cause it to lose its function of suppression of cell division.

BRCA-1 is also associated with 10-15% lifetime risk of ovarian cancer.

Another breast cancer gene BRCA-2 has been identified on the long arm of chromosome-13 and is also associated with increasd risk of developing breast and ovarian malignancies.

In inherited breast cancers other genetic defects have also been established, e.g. mutation or loss of heterozygosity of tumor suppressor gene p53 on the short arm of chromosome 17. This occurs in Li-Fraumeni syndrome in which there is increased tendency to develop soft tissue sarcoma, breast cancer, melanoma etc. when associated with ovarian and colonic cancers it is known as Lynch type 2 syndrome.

Those with Ataxia Telangiectasia syndrome also have increased risk of developing breast carcinoma, as also in Cowden's disease (multiple hamartoma syndrome) due to defective tumor suppressor gene.

Patients carrying a genetically high risk require a close surveillance i.e. physical examination every six months and mammography annually.

The situation is further complicated by the data that exposure to radiation during mammography, may increase the oncogenic risk in mutation carriers.

Prophylactic bilateral mastectomy, recommended by some in such circumstances appear too aggressive and lacks universal approval at present time

DIAGNOSTIC FACTORS IN BREAST CARCINOMA: MAMMOGRAPHY :

Mammography showing invasive breast cancer

It is a plain x ray of soft tissue of breast using a low voltage and high amperage x rays

Two films are taken

Craniocaudal from above downward

Mediolateral from side to side

Dose of radiation is 0.1Gy, so it is a safe and effective procedure.

Findings :

Microcalcifications signify malignancy

Soft tissue shadows may be smooth and regular in benign conditions and irregular in carcinomas

Size and location of mass lesions

Spiculations, duct distortion.

BIRADS GRADING IN MAMMOGRAPHY:

Grade 1 – Negative

Grade 2 – Benign lesion

Grade 3 – Probably benign lesion

Grade 4 – Suspicious of breast carcinoma

Grade 5 – Highly suggestive of carcinoma

Grade 6 – known carcinoma

INDICATIONS :

For screening purposes it is done after 40 years. Early screening is indicated when there is family history of carcinoma breast or histological risk factor. Mammography before 35 years is usually not done unless there is suspicious lump or a strong family history.

* In obese patients
* Whenever conservative breast surgeries are planned.
* To find out spread or de novo tumor in the contralateral breast.
* Mammography guided biopsy can be done.
* Evaluation and follow up in benign breast disease with malignant potential.
* Follow up mammography after conservative breast surgery.
* Mastalgias.

Digital mammography is computerised electronic image of the breast with enhanced and magnified pictures.

Digital spot view mammography allows faster and more accurate streotactic biopsy.

Mammography fails to detect 10% to 15% of all palpable malignant lesions, and its sensitivity is particularly decreased in women with lobular carcinoma or radiographically dense breast tissue.

Therefore, a negative mammogram should not influence the decision to perform a biopsy of a clinically palpable lesion.

Xeromammography is the same as above but here a photo conductor is used to produce the final image on a selenium paper rather than on a x ray film.

Advantages

Edge enhancement effect, therefore useful in dense breasts.

Disadvantages

Exposure to high radiation dose and selenium plates are needed.

ULTRASOUND BREAST :

The main value of ultrasonography is in distinguishing cystic from solid lesions.

If the lesion is not palpable, ultrasonography can determine whether the lesion is cystic and thus potentially eliminate the need for additional workup or treatment.

Ultrasonography has not proved useful for screening: it fails to detect calcifications, misses a large number of malignancies, and identifies a great deal of normal breast texture as potential nodules.

It is useful, however, for directing fine-needle or core-needle biopsy of the lesions that it does visualize: it permits real-time manipulation of the needle and direct confirmation of the position of the needle within the lesion.

MAGNETIC RESONANCE IMAGING :

Magnetic resonance imaging after injection of gadolinium contrast enhances many malignant lesions in relation to normal breast parenchyma.

To differentiate scar from recurrence

To image breasts of women with implants

To evaluate the management of axilla

To evaluate the management of recurrent disease

It is also useful in screening of women in high risk group

Irregular mass with spiculations, changes in skin and nipple, lymphedema are the findings in carcinoma breast.

MRI breast is not accurate if done within 9 months of radiotherapy

BIOPSY METHODS :

Fine needle aspiration cytology

Advantages :

Simple office procedure

Economical

Less time consuming

No scar

Does not interfere with further treatment

Limitations :

Errors in sampling, handling, processing and reading

Does not show the architecture

Not a substitute for excision biopsy

Markers (ER and PR) not routinely available

Requires experienced cytopathologist

Core cutting needle biopsy :

Advantages :

Rapid, relatively painless, inexpensive.

No incision.

Produces histological rather than a cytological diagnosis.

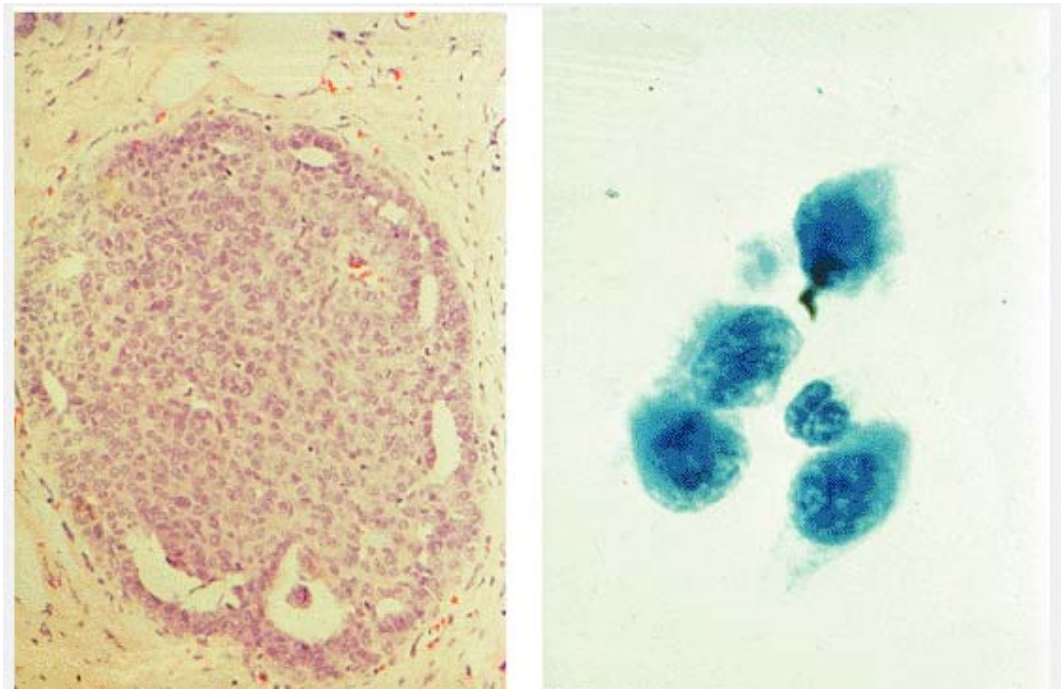
Can be read by any pathologist, markers routinely available.

Disadvantages :

False-negative results,

Incomplete lesion characterization can occur.

Difference between FNAC and core cut biopsy samples :



Excisional biopsy :

Advantages :

False-negative results rare.

Complete histology before treatment decisions.

May serve as definitive lumpectomy.

Disadvanges :

Expensive, more painful.

Creates an incision to be incorporated into definitive surgery.

Unnecessary surgery with potential for cosmetic deformity in patients with benign abnormalities.

TRIPLE ASSESSMENT :

1. History and clinical examination
2. Imaging – for patients below 40 years an ultrasound is performed, for those above 40 years mammogram is done.
3. Fine needle aspiration cytology or Core cutting needle biopsy.

METASTATIC WORK UP :

An ultrasound abdomen is done to pick up liver metastasis, krukenberg tumor and ascites.

An X-ray chest is done to see for pleural effusion, mediastinal widening and cannon ball secondary.

A bone scan for all patients with stage 3 disease, pathological fracture and elevated alkaline phosphatase.

STAGING OF BREAST CARCINOMA :

TNM STAGING :

PRIMARY TUMOR (T)

TX: Primary tumor cannot be assessed

T0: No evidence of primary

Tis: Intraductal carcinoma, lobular carcinoma in situ, or Paget's disease of the nipple

Tis (DCIS): Ductal carcinoma in situ

Tis (LCIS): Lobular carcinoma in situ

Tis (Paget's): Paget's disease of the nipple with no tumor

T1: Tumor not > 2.0 cm in greatest dimension

T1mic: Microinvasion not >0.1 cm in greatest dimension

T1a: Tumor > 0.1 cm but not >0.5 cm in greatest dimension

T1b: Tumor > 0.5 cm but not > 1.0 cm in greatest dimension

T1c: Tumor > 1.0 cm but not > 2.0 cm in greatest dimension

T2: Tumor > 2.0 cm but not > 5.0 cm in greatest dimension

T3: Tumor > 5.0 cm in greatest dimension

T4: Tumor of any size with direct extension to (a) chest wall or (b) skin,

T4a: Extension to chest wall, not including pectoralis muscle

T4b: Edema (including peau d'orange) or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast

T4c: Both T4a and T4b

T4d: Inflammatory carcinoma

REGIONAL LYMPH NODES (N)

NX: Lymph nodes cannot be assessed (e.g., previously removed)

N0: No regional lymph node metastasis

N1: Metastasis to movable ipsilateral axillary lymph node(s)

N2: Metastasis to ipsilateral axillary lymph node(s) fixed or matted, or in clinically apparent ipsilateral internal mammary nodes in the absence of clinically evident axillary nodal metastasis

N2a: Metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures

N2b: Metastasis only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastasis

N3: Metastasis in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement, or in clinically apparent ipsilateral internal mammary lymph node(s) and in the presence of clinically evident axillary lymph node metastasis; or, metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement

N3a: Metastasis in ipsilateral infraclavicular lymph node(s)

N3b: Metastasis in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)

N3c: Metastasis in ipsilateral supraclavicular lymph node(s)

PATHOLOGIC CLASSIFICATION (pN)

pNX: Regional lymph nodes cannot be assessed (e.g., not removed for pathologic study or previously removed)

pN0: No regional lymph node metastasis histologically, and no additional examination for isolated tumor cells (ITC)

[Note: ITCs are defined as single tumor cells or small cell clusters not larger than 0.2 mm, usually detected only by immunohistochemical (IHC) or molecular methods but that may be verified on hematoloxylin and eosin (H&E) stains. ITCs do not usually show evidence of malignant activity, e.g., proliferation or stromal reaction].

pN0(I-): No regional lymph node metastasis histologically, negative IHC

pN0(I+): No regional lymph node metastasis histologically, positive IHC, and no IHC cluster larger than 0.2 mm

pN0(mol-): No regional lymph node metastasis histologically, and negative molecular findings (RT-PCR)

pN0(mol+): No regionally lymph node metastasis histologically, and positive molecular findings (RT-PCR)

pN1: Metastasis in one to three axillary lymph nodes, and/or in internal mammary nodes with microscopic disease detected by SLN dissection but not clinically apparent

pN1mi: Micrometastasis (larger than 0.2 mm but not larger than 2.0 mm)

pN1a: Metastasis in one to three axillary lymph nodes

pN1b: Metastasis in internal mammary nodes with microscopic disease detected by SLN dissection but not clinically apparent

pN1c: Metastasis in one to three axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by SLN dissection but not clinically apparent. (If associated with more than three positive axillary lymph nodes, the internal mammary nodes are classified as pN3b to reflect increased tumor burden.)

pN2: Metastasis in four to nine axillary lymph nodes, or in clinically apparent internal mammary lymph nodes in the absence of axillary lymph node metastasis to ipsilateral axillary lymph node(s) fixed to each other or to other structures

pN2a: Metastasis in four to nine axillary lymph nodes (at least one tumor deposit larger than 2.0 mm)

pN2b: Metastasis in clinically apparent internal mammary lymph nodes in the absence of axillary lymph node metastasis

pN3: Metastasis in 10 or more axillary lymph nodes, or in infraclavicular lymph nodes, or in clinically apparent ipsilateral internal mammary lymph node(s) in the presence of one or more positive axillary lymph node(s); or, in more than three axillary lymph nodes with clinically negative microscopic metastasis in internal mammary lymph nodes; or, in ipsilateral supraclavicular lymph nodes

pN3a: Metastasis in ten or more axillary lymph nodes (at least one tumor deposit larger than 2.0 mm); or, metastasis to the infraclavicular lymph nodes

pN3b: Metastasis in clinically apparent ipsilateral internal mammary lymph nodes in the presence of one or more positive axillary lymph node(s); or, in more than three axillary lymph nodes and in internal mammary lymph nodes with microscopic disease detected by sentinel lymph node dissection but not clinically apparent

pN3c: Metastasis in ipsilateral supraclavicular lymph nodes

DISTANT METASTASIS (M)

MX: Presence of distant metastasis cannot be assessed

M0: No distant metastasis

M1: Distant metastasis

AJCC STAGE GROUPINGS

Stage 0

Tis, N0, M0

Stage I

T1, N0, M0

Stage IIA

T0, N1, M0

T1, N1, M0

T2, N0, M0

Stage IIB

T2, N1, M0

T3, N0, M0

Stage IIIA

T0, N2, M0

T1f, N2, M0

T2, N2, M0

T3, N1, M0

T3, N2, M0

Stage IIIB

T4, N0, M0

T4, N1, M0

T4, N2, M0

Stage IIIC

Any T, N3, M0

Stage IV

Any T, Any N, M1

Locally Advanced Breast Cancer (Stage 3)

MANCHESTER CLASSIFICATION :

STAGE 1

Tumor confined to breast tissue. Not fixed to the pectoralis major, not fixed to chest wall, no nodes in axilla, no metastasis.

STAGE 2

Tumor of any size with peau d orange, or infiltration of skin less than the size of the tumor, tumor not fixed to pectoralis major or chest wall. Axillary nodes are palpable and mobile, no metastasis.

STAGE 3

Involvement of skin or peau d orange more than the size of the tumor. Tumor fixed to pectoralis major, axillary nodes are fixed, or supraclavicular nodes are palpable, no metastasis.

STAGE 4

Chest wall fixation, involvement of opposite breast and axilla, distant metastasis in bones and lungs.

PROGNOSTIC FACTORS IN BREAST CARCINOMA :

TUMOR FACTORS :

Axillary nodal status

Tumor size

Histological / nuclear grade

Lymphatic / vascular invasion

Hormone receptor status

DNA content (ploidy, phase fraction)

Extensive intraductal component

Growth factor indicators- EGFR, Erb B2

Factors relating to tumor invasion – cathepsin d, collagenase activity

Factors relating to growth rate – p53, S-phase fraction

Factors relating to cell adhesion – Cd44 glycoprotein

HOST FACTORS :

Age

Menopausal status

Family history

Previous breast cancer

Immunosuppression

Nutrition

Prior chemotherapy

Prior radiation therapy

PROGNOSTIC FACTORS :

LYMPH NODAL METASTASIS –

The single most important prognostic indicator of the breast cancer is the ipsilateral axillary nodal status, with 4 being the magic number, above which there is dramatic reduction of long term survival.

The overall prognosis is good for node negative disease, with 75% disease free 10 year survival provided the other prognostic factors are favourable, but the survival drops to 50% if less than 4 nodes are microscopically involved, and to 25% if greater than 4 nodes are positive.

As may be expected lymphatic and vascular invasion has also been shown to be a poor prognostic factor.

Nodal involvement in contralateral axilla is considered as distant metastatic disease and hence considered Manchester stage 4 and TNM stage 4. If this is the only finding upstaging the disease to stage 4, it has to be established beyond doubt, by either FNAC or excision biopsy.

TUMOR SIZE –

Large tumors have a significantly worse prognosis, all the other factors obviously contribute to the metastatic potential of a given tumor.

The recurrence rate is significantly higher for a larger tumor, and the relapse free survival significantly lower.

From the excised specimen assessing the degree of invasive component of the breast is a better predictor of its biological behaviour than the total tumor size.

HISTOLOGICAL GRADE-

It is based on Bloom and Richardson classification system.

Grade is classified as 1, 2, 3 based on tubule formation, nuclear pleomorphism, and mitotic rate. Mitotic rate is the most powerful factor.

Grade 1- well differentiated

Grade 2 – intermediate

Grade 3 – poor differentiation

TUMOR TYPE :

A pure mucinous or papillary type has a significantly better prognosis than a comedo carcinoma or NOS type.

CELL KINETICS AND PLOIDY :

The most significant predictor of loco-regional relapse of carcinoma breast is cellular proliferation i.e, measuring the percentage of cells dividing at any given point of time and also the degree of cell division (which is shown by the nuclear grade).

Measurement of the rate of tumor cell division and the quantity of DNA (ploidy) in each cell helps to predict the course of node negative cancer.

The mitotic index (number of mitotic fiures/10HPF) has a predictive value for prognosis, with a distinctive advantage of it is <10 figures.

The DNA index and the ‘S’ phase fraction measurement by flow cytometry are quick and reliable methods of quantifying the growth characteristics of the tumor and serve as good predictors of survival and recurrence.

The main impact of cell kinetic studies is in the clinical management of node negative breast cancer.

The high ‘S’ phase fraction and aneuploidy are features that indicate a poor prognosis and adjuvant therapy would be strongly indicated in this group of patients even if node negative, as these tumors have a higher risk of locoregional recurrence.

HORMONE RECEPTORS :

Identification of the oestrogen and the progesterone receptors (ER and PR) in the tumor cells by immunohistochemistry (IHC) is helpful in the prognosis and identifying the response to hormonal therapy.

When a high level of these receptors is found it often indicates the tumor is slow growing and the prognosis consequentially better, with 90% probability of the tumor being responsive to hormonal manipulation.

The reasons for better prognosis in ER / PR positive patients are :

They are generally well differentiated and slow growing tumors.

It is considered to be an index of cellular synthetic functions, influenced by alteration of hormonal milieu.

High probability of additional weapon against the tumor (hormonal therapy) being effective.

Patients with tumors that are negative for both ER and PR have a slightly worse prognosis than those patients who have cancers with either ER or PR being positive. These data are based on NSABP-06 trial.

Her 2- neu :

Human Epidermal Growth factor receptor 2 is a tyrosine kinase receptor, which plays a major role in normal cell growth.

Over expression of Her 2 neu (an oncogene) has been correlated with more aggressive cancer. Even in node negative women with over expression of Her 2, there is a strong correlation with early recurrence.

Though initial detection is done by IHC, gene amplification is to be verified by Florescence in situ hybridization technique (FISH), to exclude false positive reporting.

Targeted therapy using monoclonal antibody directed agaist Her 2 neu receptor Trastuzumab (Herceptin) is used in these patients.

Cathepsin – D :

Cathepsins are a family of enzymes that cleave the interior bond of various proteins. Normal breast tissue contains very little cathepsin d, but

high levels are found in breast cancer tissue. The higher the cathepsin d level, the shorter the disease free interval and overall survival.

P53 :

Over expression of tumor suppressor gene p53 has been found to correlate with aggressive behaviour of tumor. This also affects radio and chemo sensitivity of the tumor, affecting the ultimate prognosis.

THERAPEUTIC ROLE OF TAMOXIFEN :

About 90% of ER / PR positive breast cancer and 10% of ER / PR negative tumors are hormone dependent. Hence the rationale in offering hormone therapy is obvious.

Tamoxifen is an antagonist of the oestrogen receptor in breast tissue via its active metabolite, hydroxytamoxifen.

In other tissues such as the endometrium, it behaves as an agonist, hence tamoxifen may be characterised as a mixed agonist / antagonist.

It has a half life of 5 – 7 days and has been standard endocrine (anti-oestrogen) therapy for hormone receptor positive breast cancer in Pre-menopausal women, while aromatase inhibitors are preferred for Post-menopausal women.

Cells of some breast cancer require oestrogen to grow. Oestrogen binds to and activates ER in these cells.

Tamoxifen is metabolised into compounds that also bind to the ER, but do not activate it. Because of this competitive antagonism, tamoxifen acts like a key broken off into a lock that prevents any other key from being inserted, preventing oestrogen from binding to its receptor. Hence breast cancer cell growth is blocked.

Tamoxifen is currently used for the treatment of both early and advanced ER positive breast cancer in Pre and Post-menopausal women. Additionally it is most common hormonal agent used in the treatment of male breast cancer. It is also advocated for the prevention of breast cancer in high risk women e.g. against cancer in contralateral breast, though the concept has not gained wide popularity.

Other anti-oestrogen compounds in use: raloxifene and anastrazole are found to be equally effective against breast cancer, but with lesser risk of developing uterine cancers and thromboembolic complications.

THERAPEUTIC ROLE OF LETROZOLE :

Letrozole is an oral non steroidal aromatase inhibitor for the treatment of hormone responsive breast cancer after surgery in Post-menopausal women.

Oestrogens are produced by the conversion of androgens by the activity of aromatase enzyme, which then binds to oestrogen receptors, stimulating cell division.

Letrozole prevents the aromatase from producing oestrogens by competitive reversible binding to the heme of its cytochrome p450 unit. This is action specific and do not interfere with the production of mineralocorticoids or glucocorticoids.

Letrozole is more effective in Post-menopausal women, in whom oestrogen is produced predominantly in the peripheral tissues (i.e. in adipose tissue and a number of sites in the brain)

Since in Pre-menopausal women the main source of oestrogen is from the ovaries and not the peripheral tissues, Letrozole is ineffective.

MATERIALS AND METHODS

This is a prospective study done in patients admitted in various wards in Rajiv Gandhi Government General Hospital,Chennai with signs and symptoms of carcinoma breast ,who were clinically evaluated and confirmed by FNAC / core-cut biopsy.

Inclusion Criteria :

Patients presenting with signs and symptoms of carcinoma breast and diagnosed by FNAC / core-cut biopsy in various wards of Rajiv Gandhi Government General Hospital,Chennai.

Exclusion Criteria :

1] Patients with benign breast disorders

2] Patients who refused any mode of therapy

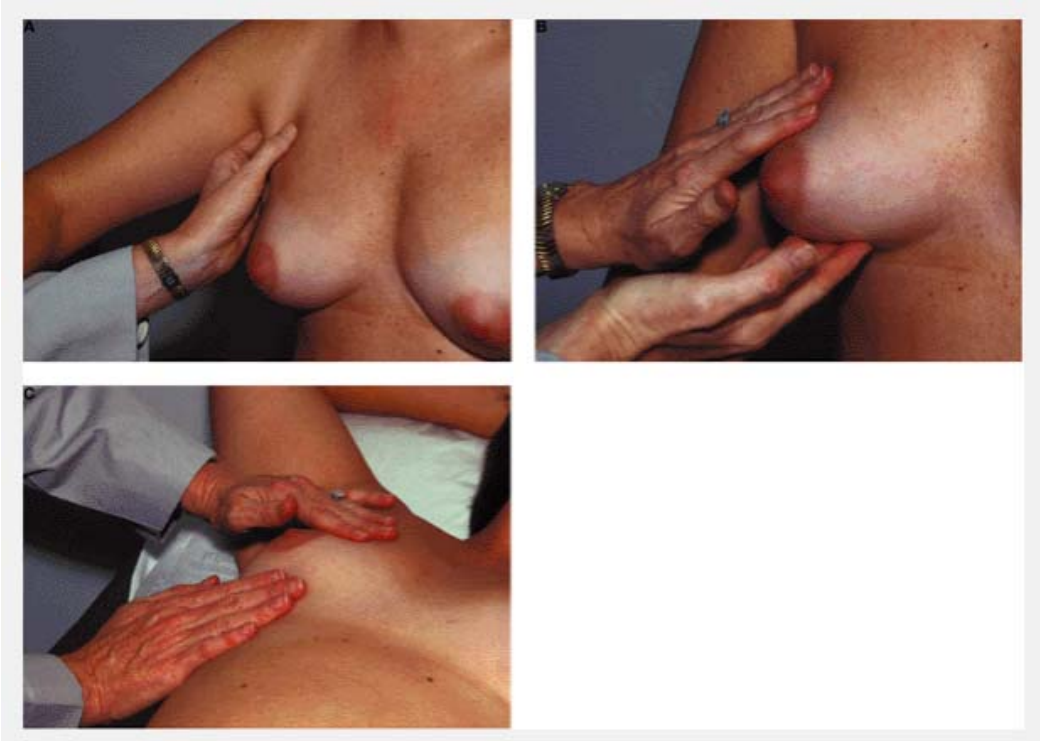
3] Patients who have been previously treated surgically for other breast ailments

Sample Size : 50 patients

Investigation Details :

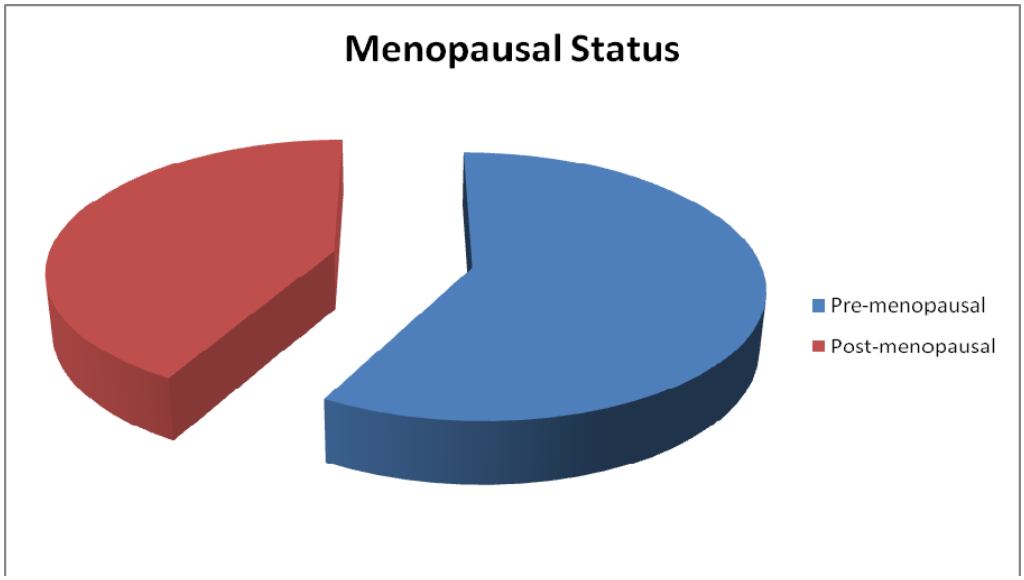
Detailed Clinical Examination, Routine Laboratory investigations, FNAC/core-cut biopsy, mammogram/USG-Breast, Chest X ray, USG-Abdomen, Skeletal survey, HPE.

EXAMINATION OF BREAST



OBSERVATION AND INFERENCE

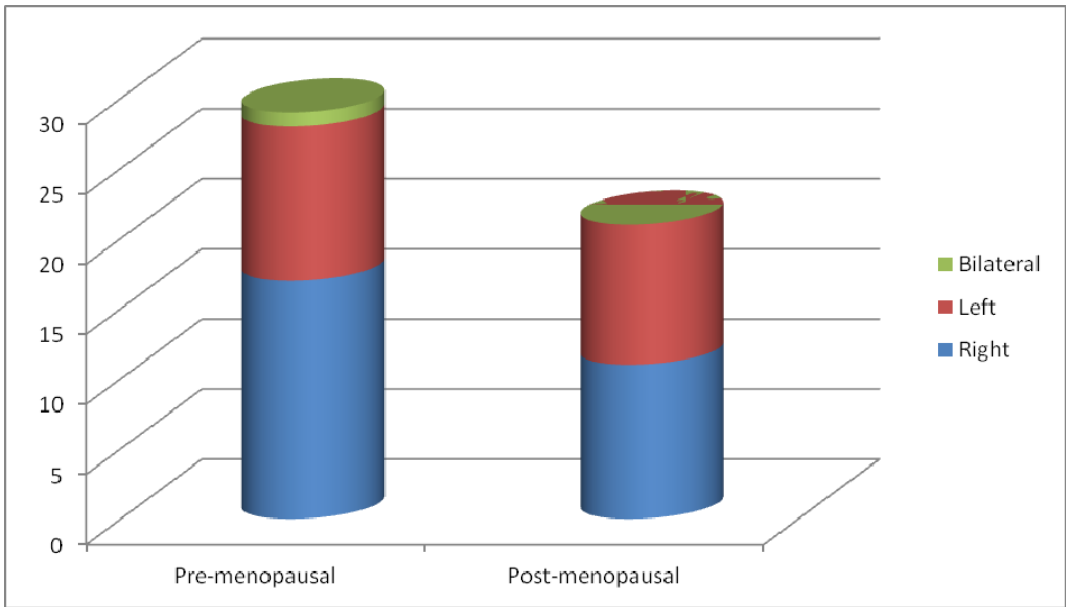
A total number of 50 cases of breast cancer reported in General Surgery department in Rajiv Gandhi Government General Hospital Chennai were taken for the study. Out of the 50 cases 29 patients were pre-menopausal and 21 patients were post-menopausal.



AGE DISTRIBUTION :

Age in years	Number of patients
21 – 30	1
31 – 40	17
41 – 50	13
51 – 60	10
61 – 70	7
71 – 80	2

LATERALITY OF BREAST CANCER

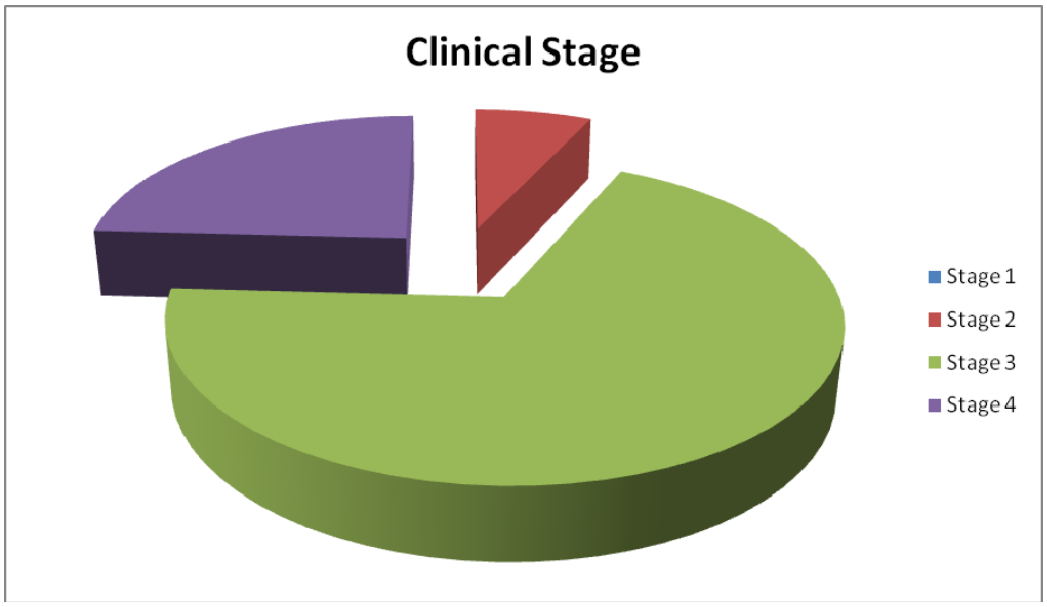


CLINICAL STAGE AT PRESENTATION :

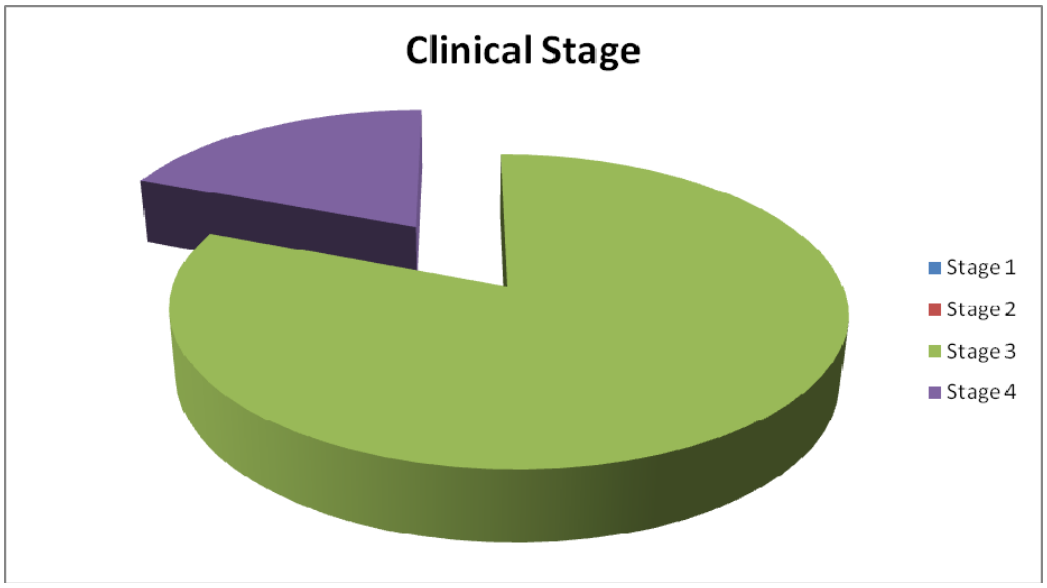
Among Pre-menopausal women 2 patients presented in stage 2B, 8 patients presented in stage 3A, 12 patients presented in Stage 3B, & 7 patients presented in stage 4.

Among Post-menopausal women 3 patients presented in stage 3A, 14 patients presented in stage 3B, & 4 patients presented in stage 4.

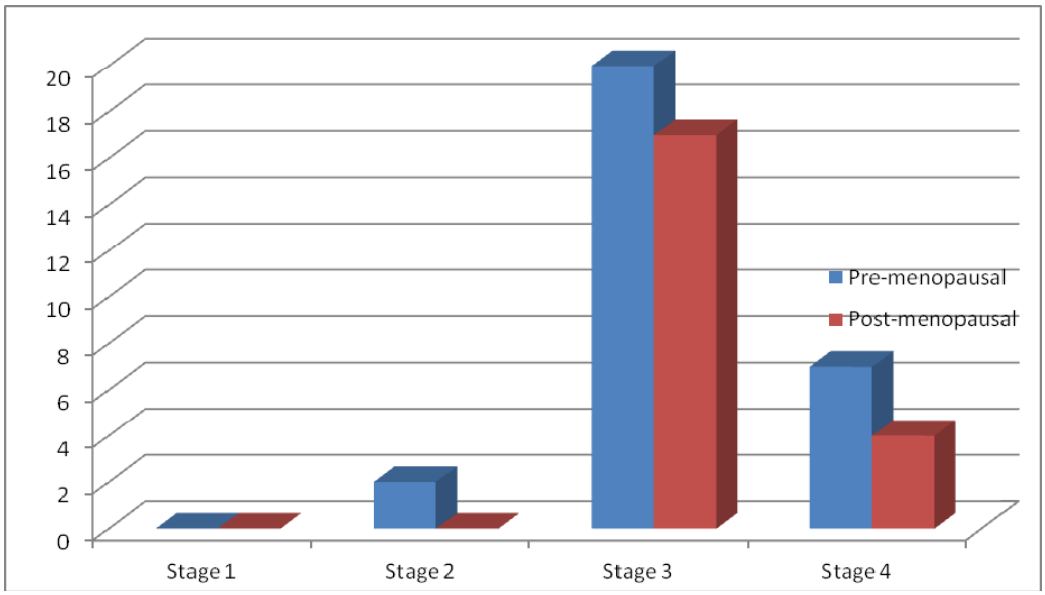
PRE-MENOPAUSAL WOMEN :



POST-MENOPAUSAL WOMEN :



COMPARISION OF CLINICAL STAGE IN PRE-MENOPAUSAL AND POST-MENOPAUSAL WOMEN :



No patients in both Pre-menopausal and Post-menopausal group presented in clinical stage 1.

6.8% of patients in Pre-menopausal group and none of the patients in Post-menopausal group presented in Stage 2.

68.96% of patients in Pre-menopausal group and 80.95% of patients in Post-menopausal group presented in stage 3.

24.13% of patients in Pre-menopausal group and 19.04% of patients in Post-menopausal group presented in stage 4.

COMPARISION OF BODY MASS INDEX (BMI) :

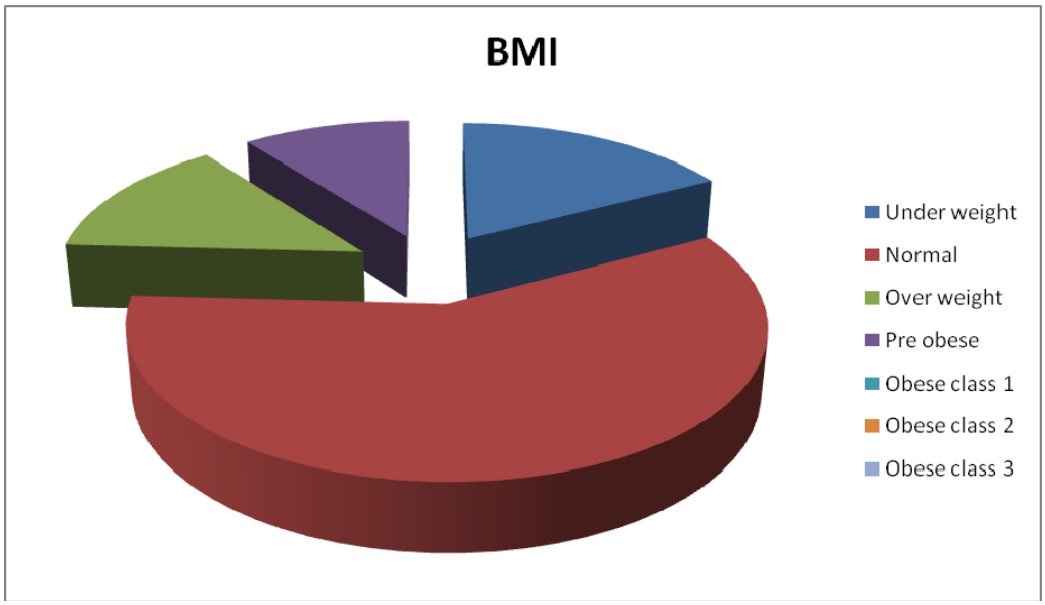
Classification of the study patients according to BMI is done as per the following table,

Classification	BMI (kg / m2)
Underweight	<18.5
Normal Range	18.5 – 22.9
Overweight	23 – 24.9
Pre Obese	25 – 29.9
Obese class 1	30 – 34.9
Obese class 2	35 – 39.9
Obese class 3	>40

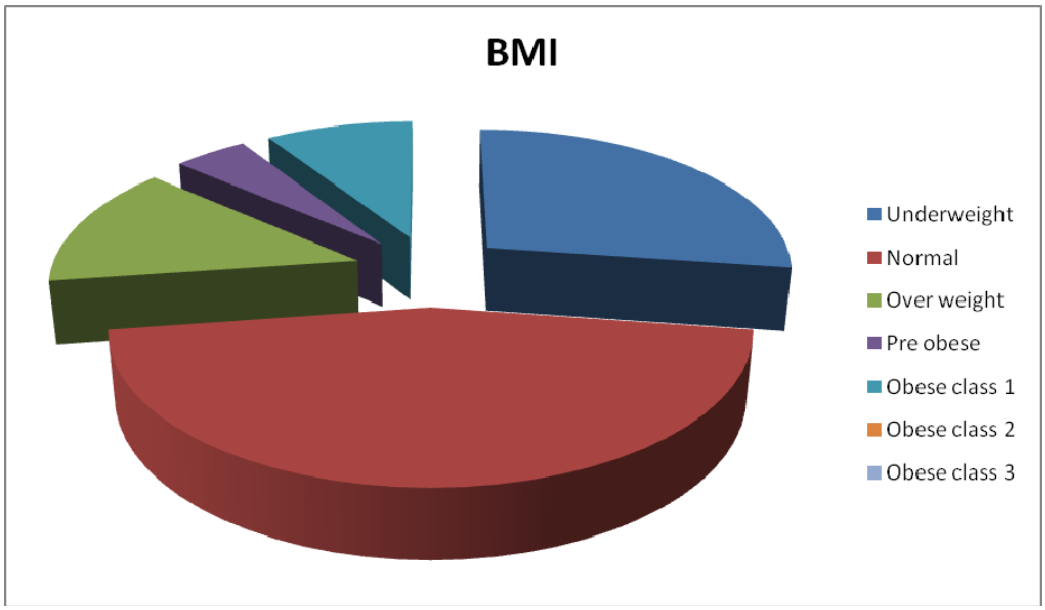
Among the Pre-menopausal patients 5 patients were underweight, 17 patients were normal, 4 patients were overweight, and 3 patients were pre-obese and none were obese.

Among the Post-menopausal patients 6 patients were underweight, 10 patients were normal, 3 patients were overweight, 1 patient was pre-obese and 2 patients were obese class-1.

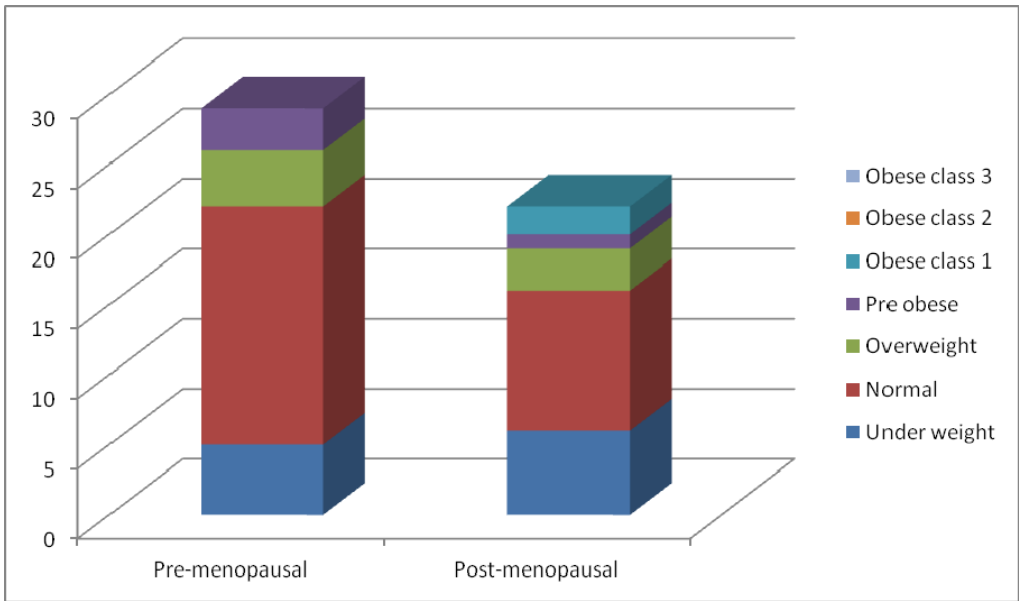
PRE-MENOPAUSAL WOMEN :



POST-MENOPAUSAL WOMEN :



COMPARISION OF BMI :



17.24% of patients in Pre-menopausal group and 28.57% of patients in Post-menopausal group were Underweight.

58.62% of patients in Pre-menopausal group and 47.61% of patients in Post-menopausal group were Normal.

13.79% of patients in Pre-menopausal group and 14.28% of patients in Post-menopausal group were Over weight.

10.34% of patients in Pre-menopausal group and 4.76% of patients in Post-menopausal group were Pre-obese.

None of the patients in Pre-menopausal group and 9.52% of patients in Post-menopausal group were Obese Class 1.

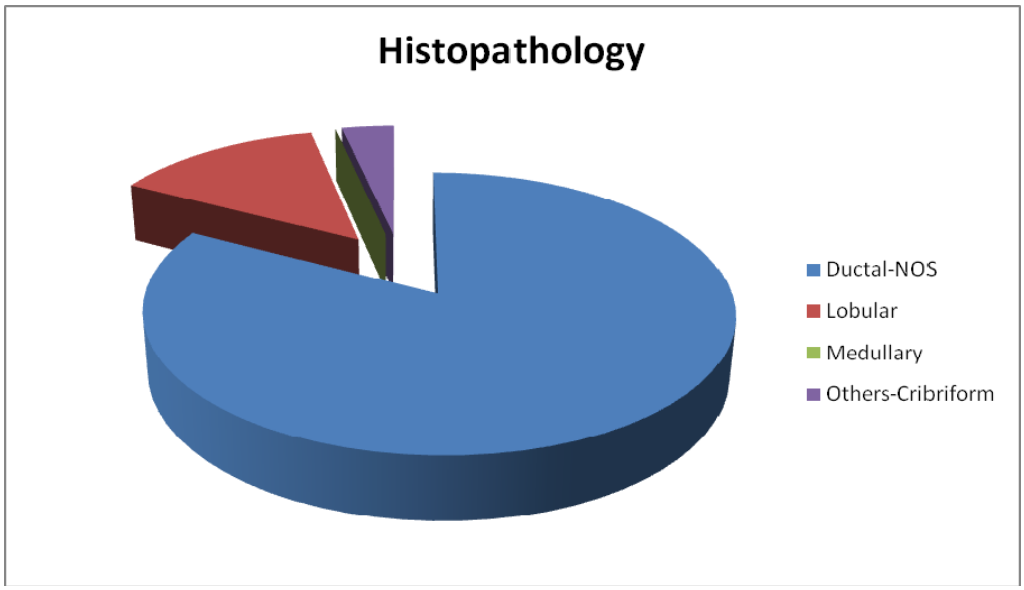
None of the patients in Pre-menopausal or Post-menopausal groups were Obese Class 2 or 3.

PATHOLOGICAL TYPES :

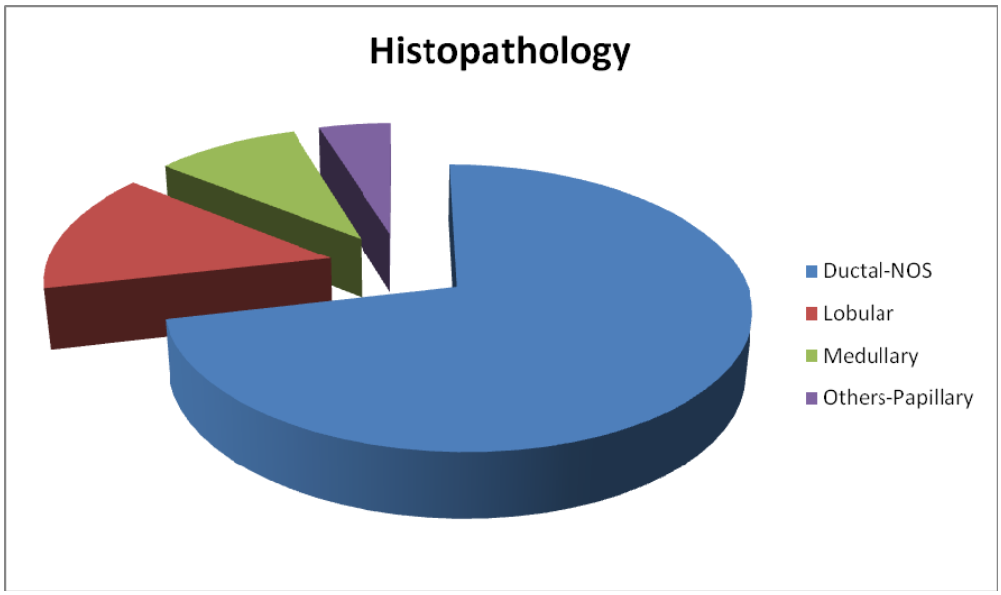
Among 29 Pre-menopausal women, 24 patients had infiltrating ductal carcinoma – NOS, 4 patients had lobular carcinoma and 1 patient had cribriform carcinoma.

Among 21 Post-menopausal women, 15 patients had infiltrating ductal carcinoma – NOS, 3 patients had lobular carcinoma, 2 patients had medullary carcinoma and 1 patient had papillary carcinoma.

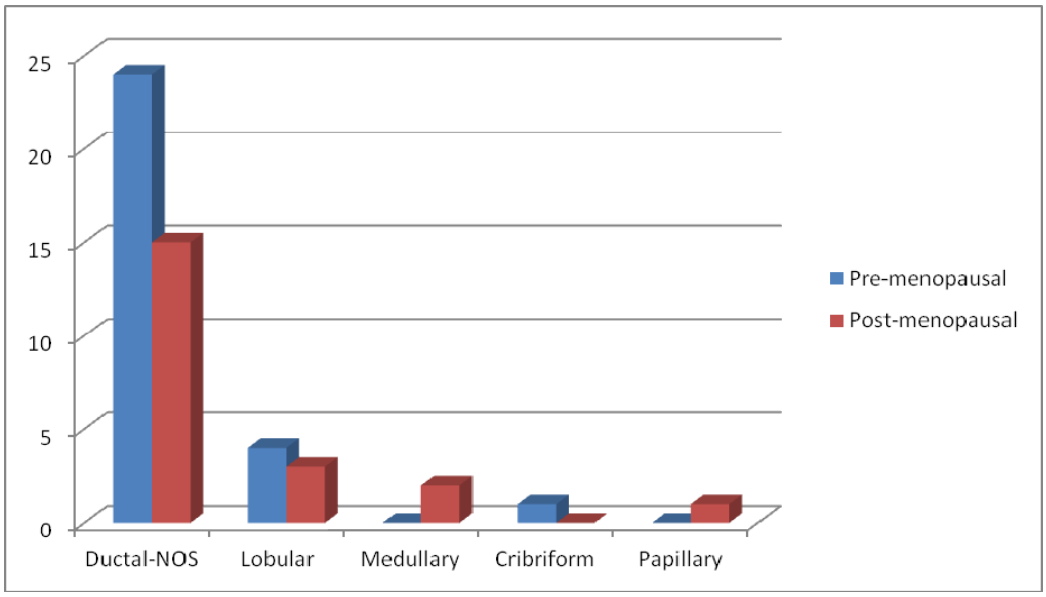
PRE-MENOPAUSAL WOMEN :



POST-MENOPAUSAL WOMEN :



COMPARISION OF HISTOPATHOLOGICAL TYPES IN PRE-MENOPAUSAL AND POST-MENOPAUSAL WOMEN :



82.75% of Pre-menopausal women and 71.42% of Post-menopausal women had histopathological type of infiltrating ductal carcinoma – NOS.

13.79% of Pre-menopausal women and 14.28% of Post-menopausal women had histopathological type of lobular carcinoma.

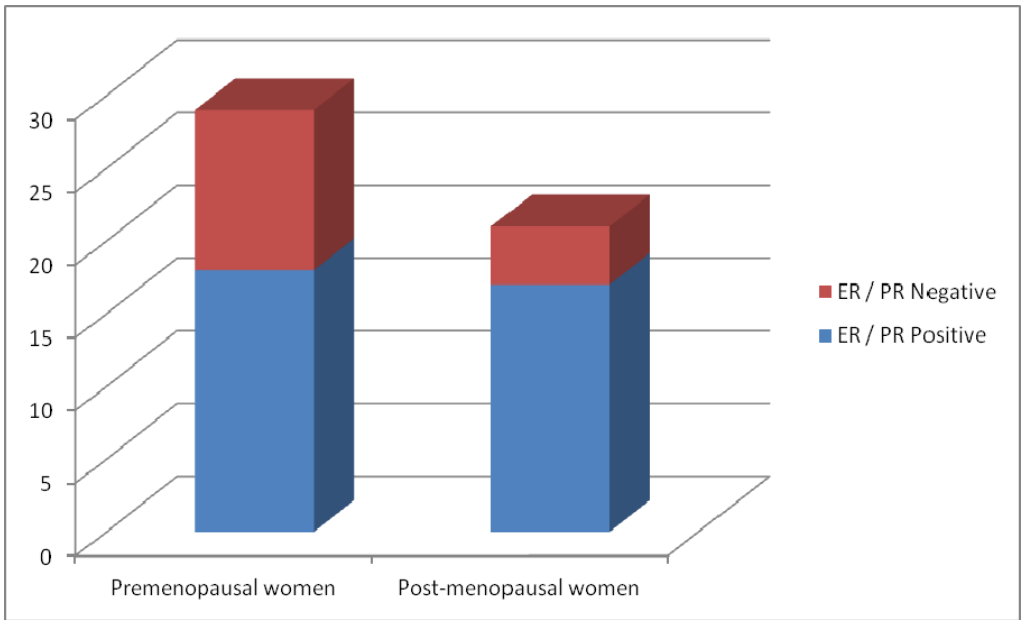
None of Pre-menopausal women and 9.5% of Post-menopausal women had histopathological type of medullary carcinoma.

Other histopathological types accounted for 3.44% in Pre-menopausal women and 4.76% in Post-menopausal women.

ER / PR STATUS :

Among Pre-menopausal women 18 patients are ER / PR positive and 11 patients are ER / PR negative.

Among Post-menopausal women 17 patients are ER / PR positive and 4 patients are ER / PR negative.



62.06% of Pre-menopausal women and 80.95% of Post-menopausal women are ER / PR positive.

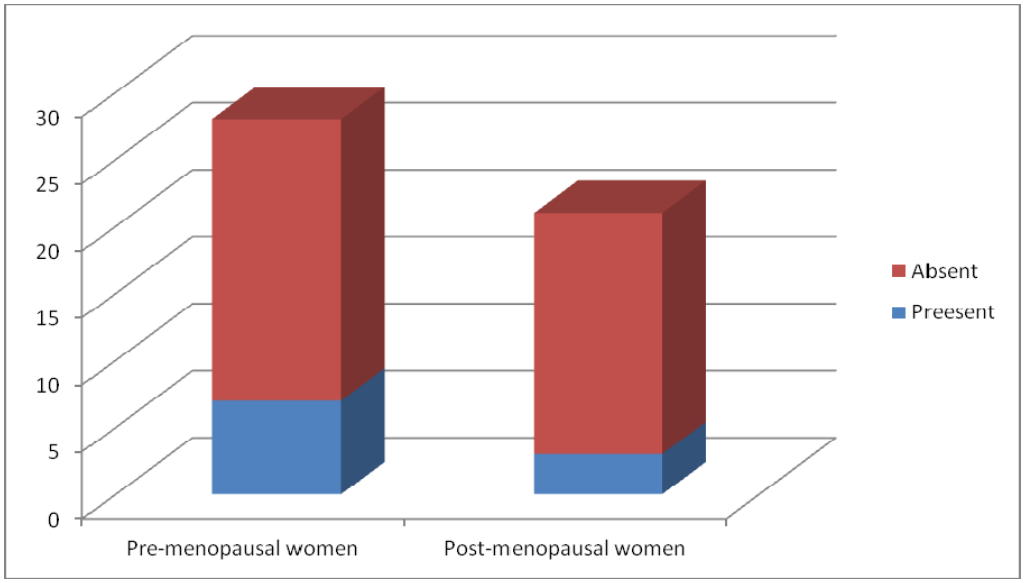
37.93% of Pre-menopausal women and 19.04% of Post-menopausal women are ER / PR negative.

ASSOCIATED PROLIFERATIVE BREAST DISEASE :

Among the 29 Pre-menopausal patients 7 patients had associated proliferative breast disease.

Among the 21 Post-menopausal patients 3 patients had associated proliferative breast disease.

PROLIFERATIVE BREAST DISEASE :



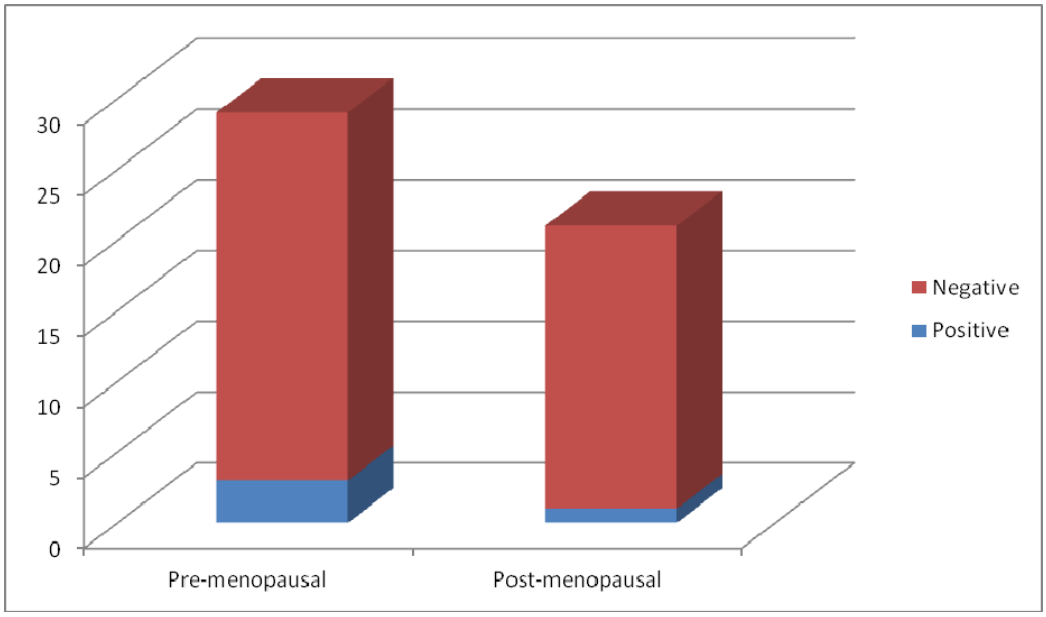
24.13% of Pre-menopausal patients had associated proliferative breast disease.

14,28% of Post-menopausal patients had associated proliferative breast disease.

MAMMOGRAPHIC ABNORMALITIES IN CONTRALATERAL BREAST :

Among 29 Pre-menopausal patients 3 patients had mammographic abnormalities in the contralateral breast out of which 2 were BIRADS 3 and 1 was BIRADS 5.

Among 21 Post-menopausal patients 1 patients had mammographic abnormality in the contralateral breast which was BIRADS 3.



10.34% of Pre-menopausal women and 4.76% of Post-menopausal women had mammographic abnormalities in contralateral breast.

The overall percentage of contralateral mammographic abnormality was 8% taking into account both Pre-menopausal and Post-menopausal groups.

DISCUSSION

This study aims at comparing various parameters in carcinoma breast in Pre-menopausal and Post-menopausal women and inferring the compared parameters among 50 patients in our General Surgery department.

In my study comprising 50 patients, 29 patients were Pre-menopausal and 21 patients were Post-menopausal.

As the Clinical stage at presentation to the surgical department increases, the 5 year overall and disease free survival decreases. Majority of patients in Pre-menopausal group and all the patients in Post-menopausal group presented in stage 3 (Locally Advanced Breast Cancer) and stage 4 (Metastatic Breast cancer). On comparing both the groups the proportion of patients presenting in advanced stage 3 or 4 is higher in Post-menopausal group than Pre-menopausal group.

Obesity is a significant risk factor for the development of Post-menopausal breast cancer possibly due to production of oestrogen from extra gonadal sites particularly adipose tissue. Obesity is also a protective factor against the development of breast

cancer in Pre-menopausal women possibly as a result of decreased exposure to oestrogen which in turn is due to increased number of irregular menstrual cycles. Increase in BMI (Body Mass Index) is directly proportional to increased risk of developing breast carcinoma. There is a 4% increase in odds of Post-menopausal breast cancer for every 1 kg/m^2 increase in BMI.

BMI > 31.1 has 2.5 fold increased risk. Taking 31.1 as cut off value, none of the women in Pre-menopausal group and 2 women in the post-menopausal group were above the cut off value. The proportion of patients with obesity is higher in the Post-menopausal group.

Histopathological type of carcinoma breast also carries prognostic significance with Invasive ductal carcinoma – NOS having a poor prognosis compared to Invasive lobular carcinoma and all other special types of cancer breast (medullary, papillary, cribriform etc.). In my study Infiltrating ductal carcinoma – NOS was the most common histopathological type of breast cancer in both Pre-menopausal and Post-menopausal groups, but the proportion of Invasive lobular carcinoma and other special histopathological types of breast cancer was higher in Post-menopausal women.

ER / PR positivity is present in 70% of patients with breast cancer. ER / PR positivity is more common in older Post-menopausal women. Oestrogen deprivation therapy using tamoxifen / aromatase inhibitors are more effective in older Post-menopausal women than younger Pre-menopausal women due to the absence of oestrogen produced from the ovaries. In my study the proportion of ER / PR positivity is higher in Post-menopausal women compared to Pre-menopausal women.

Women with proliferative breast disease have approximately twice the risk of developing carcinoma breast, regardless of menopausal status, when compared with women from general population. Proliferative disease of breast are more common in Pre-menopausal women. Post-menopausal women with senile involution of breast lacking proliferative activity have decreased risk for the development of breast cancer. In my study the proportion of patients with proliferative breast disease was higher in Pre-menopausal group compared to Post-menopausal group.

The proportion of contralateral in situ disease has increased from 5% to 33% with the use of mammography. In my study the proportion of patients with contralateral mammographic abnormality was higher in Pre-menopausal group compared to Post-menopausal group and the overall incidence was 8%.

CONCLUSIONS

1. Majority of women in both Pre-menopausal and Post-menopausal groups presented at an advanced clinical stage (stages 3 and 4), the proportion of Post-menopausal women higher than the Pre-menopausal women.

2. Incidence of obesity is higher in Post-menopausal women with breast cancer signifying positive correlation between Post-menopausal obesity and development of breast cancer.

3. Infiltrative ducal carcinoma – NOS was the most common histopathological type of breast cancer in both the groups. But the proportion of Invasive lobular carcinoma and other special types of carcinoma breast having better prognosis is common among Post-menopausal women.

4. The proportion of ER /PR positivity is higher among Post-menopausal women and hence a better prognosis, as these patients are capable of hormonal manipulation using adjuvant endocrine therapy.

5. The proportion of associated proliferative breast disease was higher in Pre-menopausal patients, hence they are at increased risk of developing contralateral breast cancer in future.

6. The overall incidence of contralateral mammographic abnormality was 8% and the proportion is higher in Pre-menopausal women compared to Post-menopausal women.

PROFORMA

Name

Age / sex

Weight, Height & BMI

Occupation

Chief complaints-

History of presenting illness-

Presence of lump

Which side ?

Site, Duration

Change in size of the lump- gradual or sudden

Any pain or fever associated

Trauma

Discharge from nipple

Skin changes

Lump in axilla

Arm oedema

Bony pain, history of jaundice, history of breathlessness

PAST HISTORY

Previous benign breast lump excision

Irradiation to breast

MENSTRUAL HISTORY

Date of menarche

Date of menopause

Last menstrual period

Cycles regular / irregular

Amenorrhoea, menorrhagia, dysmenorrhoea

OBSTETRIC HISTORY

Age at first child birth

Number of children

Breast feeding and duration

Use of oral contraceptive pills

Consanguineous or non-consanguineous marriage

PERSONAL HISTORY

Loss of weight

Loss of appetite

Loss of sleep

Bowel and bladder habits

FAMILY HISTORY

Similar history in the family

CLINICAL EXAMINATION

GENERAL EXAMINATION

Pallor, icterus, lymphadenopathy, pedal oedema

Pulse rate

Blood pressure

Respiratory rate

Temperature

Skull and spine and ends of long bones

Per abdomen

Ascites

Hepatomegaly

Krukenberg tumor

Cardio vascular system- Heart sounds

Respiratory – Breath sounds and altered sounds, pleural effusion

INSPECTION

Patient in sitting position arms by the side

Both breasts look symmetrical / asymmetrical

Both nipple at same level or not

Retraction of the nipple

Discharge from nipple

Ulceration over nipple areola complex

Peau d’orange over the areola

Dimpling or puckering

Any fullness or lump seen in any quadrant

Site, size shape, surface, all margins well defined or not

Arms above the head

Inframammary fold

Nipple retraction

Puckering or dimpling of skin

On bending forward

If both breasts falling forward equally

Opposite breast, opposite axilla, oedema of the arm

PALPATION

Normal breast is palpated first

Diseased breast-

Warmth, tenderness, site, size, shape, surface, consistency and borders of the lump

Skin pinchability

On putting the pectoralis major into contraction-

Move the lump along the fibres and then across the fibres

Moving with the breast tissue or independent of the breast tissue

Axillary nodes are palpated – anterior, posterior, central and apical groups

Site, size, number of nodes palpable, consistency, tenderness, fixed or discrete.

PERCUSSION

Internal mammary nodes in 2nd, 3rd and 4th intercostal spaces

OTHER SYSTEMS

CLINICAL

STAGING

INVESTIGATIONS

Fine needle aspiration cytology

Mammography

Chest x ray

Ultrasound abdomen

SURGERY

Modified radical mastectomy

HISTOPATHOLOGY

ER, PR STATUS by immune-histochemistry

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NAME	AGE	SEX	MENOPAUSAL STATUS	LATERALIT	IP NO	CLINICAL STAG	BMI	HPE	ER / PR	PROLIFERATIVE DISEASE	BIRADS
Vijayalakshmi	38	F	Pre-menopausal	Right	113932	3A	21.4	Ductal-NOS	Positive	Positive	1
Latha	32	F	Pre-menopausal	Right	113904	3B	18.2	Ductal-NOS	Negative	Negative	1
Munikannamma	61	F	Post-menopausal	Left	103185	3B	19.2	Medullary	Positive	Negative	1
Kala	62	F	Post-menopausal	Left	96601	4	18.3	Ductal-NOS	Negative	Negative	1
Pitchaiammal	48	F	Pre-menopausal	Right	96522	3B	18.7	Ductal-NOS	Negative	Negative	1
Usha	35	F	Pre-menopausal	Right	84088	3B	18.5	Ductal-NOS	Positive	Negative	1
Radha bai	80	F	Post-menopausal	Right	81691	3B	19	Ductal-NOS	Positive	Negative	1
Padma	40	F	Pre-menopausal	Right	81711	3A	24.1	Lobular	Positive	Negative	1
Govindammal	40	F	Pre-menopausal	Right	99291	3B	26.3	Ductal-NOS	Negative	Positive	1
Savithri	45	F	Pre-menopausal	Left	68924	4	21.3	Ductal-NOS	Positive	Positive	3
Aisha bee	75	F	Post-menopausal	Right	67655	3B	18.9	Ductal-NOS	Positive	Negative	1
Kamala	55	F	Post-menopausal	Left	64310	3B	18.8	Lobular	Positive	Negative	1
Nagamani	45	F	Pre-menopausal	Right	61831	4	18.4	Ductal-NOS	Negative	Negative	1
Krishnaveni	50	F	Post-menopausal	Right	57336	3A	19.8	Ductal-NOS	Negative	Positive	1
Kuppammal	47	F	Post-menopausal	Left	54906	3B	19.7	Ductal-NOS	Positive	Negative	1
Parameshwari	40	F	Pre-menopausal	Left	25464	3B	23.2	Lobular	Positive	Negative	1
Parvathy	65	F	Post-menopausal	Left	27726	3A	19.4	Ductal-NOS	Positive	Negative	1
Lakshmi	58	F	Post-menopausal	Right	31754	3B	32.4	Ductal-NOS	Positive	Negative	1
Pappammal	62	F	Post-menopausal	Right	40690	3B	18.3	Ductal-NOS	Positive	Negative	1
Latha	42	F	Pre-menopausal	Left	43106	3B	28.5	Ductal-NOS	Positive	Negative	3
Dhanalakshmi	35	F	Pre-menopausal	Right	94312	2B	27.2	Ductal-NOS	Positive	Negative	1
Jamuna	55	F	Post-menopausal	Left	99566	3B	24.9	Ductal-NOS	Positive	Negative	1
Saroja	50	F	Pre-menopausal	Right	97088	4	24	Lobular	Positive	Negative	1
Kavitha	44	F	Pre-menopausal	Right	84181	3A	20.3	Ductal-NOS	Positive	Negative	1
Govindammal	30	F	Pre-menopausal	Right	86074	2B	20.7	Ductal-NOS	Negative	Negative	1
Poongodi	44	F	Pre-menopausal	Right	86877	3B	18.4	Ductal-NOS	Positive	Negative	1

Saraswathi	54	F	Post-menopausal	Right	74883	4	23.2	Lobular	Negative	Negative	1
Sengammal	52	F	Post-menopausal	Left	74844	3B	18.4	Ductal-NOS	Negative	Positive	1
Padma	31	F	Pre-menopausal	Right	74233	4	21.9	Ductal-NOS	Positive	Negative	1
Ahila	40	F	Pre-menopausal	Right	76952	4	20.5	Ductal-NOS	Negative	Negative	1
Kumari	55	F	Post-menopausal	Left	77436	3B	24.3	Medullary	Positive	Negative	1
Kondamma	39	F	Pre-menopausal	Left	79771	3A	18.6	Ductal-NOS	Positive	Negative	1
Natchiyammal	35	F	Pre-menopausal	Right	80036	3A	18.3	Ductal-NOS	Positive	Positive	1
Vijayalakshmi	35	F	Pre-menopausal	Left	77475	3B	18.4	Lobular	Positive	Negative	1
Jeyanthi	44	F	Pre-menopausal	Left	80602	3B	19.3	Ductal-NOS	Negative	Negative	1
Rajeshwari	68	F	Post-menopausal	Right	81691	4	19.1	Papillary	Positive	Positive	1
Padmavathi	48	F	Pre-menopausal	Left	81761	3B	18.1	Ductal-NOS	Positive	Negative	1
Lakshmi	54	F	Post-menopausal	Right	80252	3A	21.3	Ductal-NOS	Positive	Negative	1
Andal	58	F	Post-menopausal	Left	78897	3B	27.8	Ductal-NOS	Positive	Negative	1
Visalakshi	65	F	Post-menopausal	Right	81627	3B	18.7	Ductal-NOS	Positive	Negative	1
Varagu	50	F	Pre-menopausal	Left	77062	3A	23.5	Ductal-NOS	Negative	Negative	1
Logeshwari	40	F	Pre-menopausal	Bilateral	77644	4	20.9	Ductal-NOS	Negative	Positive	5
Neela	39	F	Pre-menopausal	Right	81987	3B	22.3	Ductal-NOS	Positive	Negative	1
Sarala	55	F	Post-menopausal	Left	81904	3B	31.3	Ductal-NOS	Positive	Negative	1
Raniyammal	72	F	Post-menopausal	Right	82000	4	19.6	Ductal-NOS	Positive	Negative	1
Lakshmi	32	F	Pre-menopausal	Left	62156	3A	19.4	Lobular	Negative	Negative	1
Ambika	60	F	Post-menopausal	Right	61518	3B	18.4	Ductal-NOS	Positive	Negative	3
Jeyanthi	42	F	Pre-menopausal	Left	59988	3A	21.1	Ductal-NOS	Positive	Positive	1
Pushpa	39	F	Pre-menopausal	Right	58168	4	18.4	Cribriform	Positive	Positive	1
Farzana	42	F	Pre-menopausal	Left	57186	3B	18.6	Ductal-NOS	Negative	Negative	1